

W
6
3

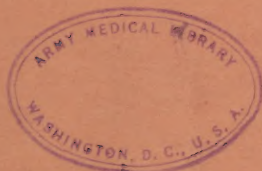
2063
no. 11

SYMPOSIUM ON THERAPY

PUBLISHED
BY THE
MASSACHUSETTS DEPARTMENT
OF MENTAL HEALTH



SEPTEMBER, 1939



SYMPOSIUM ON THERAPY

PUBLISHED
BY THE
MASSACHUSETTS DEPARTMENT
OF MENTAL HEALTH

EDITED UNDER THE PROVISIONS OF SECTION 11, CHAPTER 123,

GENERAL LAWS, BY
CLIFTON T. PERKINS, M.D.



SEPTEMBER, 1939

PUBLICATION OF THIS DOCUMENT APPROVED BY THE COMMISSION ON ADMINISTRATION AND FINANCE
1200. 5-39. No. 7087.

OCCUPATIONAL PRINTING PLANT
DEPARTMENT OF MENTAL HEALTH
GARDNER STATE HOSPITAL
EAST GARDNER, MASS.

CONTENTS

	PAGE
Introduction	4
The Use of Sodium Amytal Combined with Psychotherapy in Non-Cooperative and Cataleptic Patients	5-8
FERNAND LONGPRE, M.D.	
Discussion	9-10
Insulin Treatment and Psychotherapy in Chronic Dementia Praecox Patients	11-16
MALCOLM J. FARRELL, M.D.	
ETAM VASSAF, M.D.	
Discussion	17-19
Significance of Behavior During Hypoglycemia	21-22
CONRAD WALL, M.D.	
Discussion	23
The Use of Metrazol in the Treatment of Schizophrenia	25-29
HARRY MICHAELSON, M.D.	
Discussion	29-32
Treatment of the Total Organism in Schizophrenic Patients	33-37
WILLIAM CORWIN, M.D.	
JOHN W. THOMPSON, M.D.	
Discussion	37-39
Narcosis Treatment in the Psychosis	41-46
WALTER E. BARTON, M.D.	
Discussion	46-47
Benzedrine Sulphate—An Antidote for the Untoward Hypnotic and Ataxic Effects of Phenobarbital in the Treatment of Epilepsy	49-55
BENJAMIN COHEN, M.D.	
ABRAHAM MYERSON, M.D.	
Discussion	55-56
Intravenous Paraldehyde Narcosis for Pneumoencephalography	57-61
LEON J. ROBINSON, M.D.	
Discussion	61-62
The Attention Defect in Schizophrenia, Its Gradations and Therapeutic Implications	63-67
B. H. FLOWER, M.D.	
BENJAMIN COHEN, M.D.	
Discussion	67-69



SYMPOSIUM ON THERAPY
WORCESTER STATE HOSPITAL

May 18, 1938

Dr. Harry C. Solomon, Boston Psychopathic Hospital, Chairman.

FORENOON SESSION

The Use of Sodium Amytal Combined with Psychotherapy in Non-Coöperative and Cataleptic Patients

Fernand Longpre, M.D., Northampton State Hospital, Northampton.

Insulin Treatment and Psychotherapy in Chronic Dementia Praecox Patients

Malcolm J. Farrell, M.D., and Etem Vassaf, M.D., Metropolitan State Hospital, Waltham.

Significance of Behavior during Hypoglycemia

Conrad Wall, M.D., Worcester State Hospital, Worcester.

The Use of Metrazol in the Treatment of Schizophrenia

Harry Michelson, M.D., Northampton State Hospital, Northampton.

AFTERNOON SESSION

Treatment of the Total Organism in Schizophrenic Patients

William Corwin, M.D., and John W. Thompson, M.D., Metropolitan State Hospital, Waltham.

Narcosis Treatment in the Psychoses

Walter E. Barton, M.D., Worcester State Hospital, Worcester

Benzedrine Sulphate—An Antidote for the Untoward Hypnotic and Ataxic Effects of Phenobarbital in the Treatment of Epilepsy.

Benjamin Cohen, M.D., and Abraham Myerson, M.D., Grafton State Hospital, North Grafton.

Intravenous Paraldehyde Narcosis for Pneumoencephalography

Leon J. Robinson, M.D., Monson State Hospital, Palmer.

The Attention Defect in Schizophrenia, Its Gradations and Therapeutic Implications

Bardwell H. Flower, M.D., Grafton State Hospital, North Grafton.

SYMPOSIUM ON THERAPY

INTRODUCTION

DR. WM. A. BRYAN (*Superintendent, Worcester State Hospital*): I hope you will not gauge the warmth of our welcome by the brevity of what I shall say. I greet you on behalf of the hospital staff and hope that you will find this a very profitable meeting. The Acting Commissioner of the Department of Mental Diseases is with us today, and it is with great pleasure that I present to you Dr. Clifton T. Perkins,* Acting Commissioner of the Department of Mental Diseases.

DR. CLIFTON T. PERKINS: I came up here to learn something and you came to hear those who are on the program and not to hear me. I do, however, wish to present, though very briefly, the greetings of the Department and to point out that this meeting today is a first step in a program where we are trying to correlate research on clinical activities and the results of such activities in the hospitals under the jurisdiction of the Department. It is only fitting that we should come to the Worcester State Hospital as the first meeting-place for this symposium. The value of research and the value of the findings that have come out of your clinical work in past years is immeasurable. You will hear of that from those who are on the program. It is hoped, however, that the type of symposium that is presented today may be presented again at a later date and may eventually become a permanent part of the yearly program of the Department. With these few words I simply wish to turn the meeting back to Dr. Bryan and to thank him and his hospital staff as our hosts today. Thank you.

DR. BRYAN: The Chairman of this meeting and Presiding Officer is Dr. Harry Solomon, Chief of Therapeutic Research at the Psychopathic Hospital. Dr. Solomon needs no introduction to this group, and I therefore turn the symbolic gavel over to Dr. Harry Solomon. Take it away, Doctor.

DR. HARRY C. SOLOMON (*Boston Psychopathic Hospital*): The fact that there are so many here who are not compelled either by the Commissioner or by their Chiefs indicates, I think, fairly clearly that there is a great deal of interest today in the matter of therapy in regard to mental disorders. Certainly the leaven that has been given to the matter by insulin treatment and by metrazol, preceded by amytal, CO₂, and other methods of that sort, is very healthy. If I may steal the phrase from someone who just gave it to me, if these methods do nothing else, if they do little in the long run for the patients, they certainly have done an enormous amount for the doctors, because they have awakened a new interest, I am sure, in the matter of clinical therapeutic attacks, upon investigative methods and all the laboratory and modern methodology in medicine.

The first paper on this symposium is on "The Use of Sodium Amytal Combined with Psychotherapy in Non-coöperative and Cataleptic Patients," by Dr. Fernand Longpre of the Northampton State Hospital.

*Now Commissioner of the Department of Mental Health.

THE USE OF SODIUM AMYTAL COMBINED WITH PSYCHOTHERAPY
IN NON-COÖPERATIVE AND CATALEPTIC PATIENTS

By FERNAND LONGPRE, M.D.
Northampton State Hospital

Barbituric acid derivatives are exactly thirty-five years old and were first accepted by our American pharmacopeia in 1903 (1) when Fischer and von Mering demonstrated that one hundred or so barbituric acid derivatives had practical hypnotic effects. Up to 1920, however, and I should say 1923 (2), such derivatives were exclusively used for experimental, surgical, and obstetrical work and it is not until later that the psychiatric literature makes mention of a therapeutic approach through barbituric acid derivatives and especially sodium amytal, in which I have been particularly interested. In his article *Production of Sleep and Rest in Psychotic Cases*, published in the *Archives of Neurology and Psychiatry*, W. J. Bleckwenn (3) says: "For the past ten years at the Wisconsin Psychiatric Institute many drugs have been studied under the direction of Dr. W. F. Lorenz, especially those that might be effective in acute mental excitements and agitated depressions."

About the same time German psychiatrists reported beneficial results with other barbituric acid derivatives and many other authors (4) confirmed the findings, making it a fairly unanimous opinion that prolonged narcosis was a valuable sort of agent toward a temporary abortion of mental symptoms. The description of their results was slightly different. Some stressed the displacement of inhibitory phenomena in their patients, several confined their observations to the description of the narcotic manifestations, and a few mentioned the physical changes associated with the mental aspects; but everyone praised prolonged narcosis and considered it a therapeutic agent of value. In the course of the past ten years we all used it advantageously, not only for the benefit of patients to whom it was administered, but on a much larger scale especially as a remarkable asset in improving the environment of the subjects treated. Through its use we have quieted our hospitals, ameliorated sleeping conditions, and decreased the number of our daily injuries through accidents and altercations, etc.

Drs. William H. Foley and Vincent P. Rossignoli (5) of the Psychiatric Department of the Chapin Hospital in Providence, R. I. recently published an article, *Sodium Amytal as a Substitute for Tube Feeding*, which amazed me and stimulated my sense of research. At that time we were tube feeding exactly five patients daily on the Female Service, three cases of Schizophrenia of long standing, one case of Manic Depressive Psychosis, Stuporous type, of two months' duration, and a case of Involution Psychosis with morbid and nihilistic ideas of a hypochondriacal character and compulsive trends toward self-destruction. The methods as described by Drs. Foley and Rossignoli were established at once and most radically. The tube feedings were stopped and the personnel was instructed as to our attempts to replace tube feedings by stimulation toward spontaneous food intake through the use of sodium amytal. Within twenty-four hours the results were decidedly encouraging.

Because of the limited time allowed for this paper and lack of opportunity to compile all the cases which I have treated with sodium amytal in the course of the past eight months, I have decided to summarize only one case, probably one of the most striking of my series, which illustrates clearly the potential assets of barbituric acid derivatives in treating two of the most outstanding phenomena of a catatonic character, i. e., mutism and refusal of food. I shall afterwards mention some of the check-up methods which I used in order to prove that sodium amytal should really be credited with the beneficial results obtained in the following case:

Mary G., 31 upon admission, was born in Poland of average stock and came to the United States at the age of 9 after an uneventful infancy and childhood and two years' schooling in an ordinary Polish school. She landed in Brooklyn, N. Y., where she continued to go to school up to the age of 13, when she reached the 5th grade. She then moved to Springfield, Mass. where she worked as a domestic and shop employee up to the age of 18, when she was married. In the course of the following eight years she had three children and her marital life was apparently normal although greatly influenced by her personality structure, which was described by her husband as of the introvert type. Objectively, she displayed asthenic features and according to the anamnesis was, throughout her entire life, inclined to be shy, seclusive, overly devout religiously, and self-absorbed.

The onset of her psychosis was in connection with her schizoid traits which have already been brought out. It developed insidiously with a background of frightening hallucinatory contacts, vague delusional trends, feelings of unreality, and

general personality let-down. After several months she was admitted to the hospital a full-fledged schizophrenic. She kept herself withdrawn from reality, displayed emotional blunting, but talked a bit for four and a half months, then became mute and refused to eat. Tube feeding was then instituted. When I first saw this patient in November, 1935 she was still being mechanically fed, but had about preserved her initial weight. She looked like a mummy, showed stereotyped mannerisms, retained her saliva until her cheeks became bulged out and then let it out in voluminous bubbles. (She was an artist at this.) She never talked, kept her eyes tightly closed, and was tube fed. She continued to be fed until December 2, 1937 when sodium amylal treatment was attempted.

This first procedure was a revelation. Within four minutes after the administration of the medicine ($7\frac{1}{2}$ grs. intramuscularly), Mary opened her eyes, looked around, scrutinized her environment, displayed apprehension, mumbled a few words, and accepted liquid food at once. Of all the cases treated, this was certainly the prize one. The fact that she has been mechanically fed for so many years had produced many organic changes of the entire digestive channel. Mary was a baby as far as eating was concerned and she had to be re-educated and re-trained. This process was of a relatively short duration and within three days she was able to masticate solid food such as bread, potatoes and meat. In the course of the few subsequent days she displayed a great many emotions, at times cried, and occasionally became impulsive toward the personnel or the audience interested in the therapeutic measures. Gradually she began to eat an occasional meal without any medication whatsoever, and actually continued to so do until February 7, 1938 (i.e., 3 mos.) when she unfortunately contracted lobar pneumonia and died.

The results obtained were very interesting indeed, but not unexpected and simply paralleled the literature on sodium amylal in treatment of mechanically fed patients, and Mary's death, which was certainly deplorable and darkens the picture somewhat, was not at all considered as being due to the patient's new vegetative status, but simply a coincidental occurrence.

In addition to the above-mentioned stimulation of food intake under narcotic influence, we simultaneously obtained in this case a psychic ventilation of a most instructive nature which also corroborates the literature in regard to sodium amylal as a psycho-cathartic agent in mute patients and gave us definite clues as to the reason why Mary refused to eat for all of those years. As I described previously, she simply displayed apprehension and mumbled a few words when she was given sodium amylal for the first time. On the second occasion she really became threatening and aggressive and said to the physicians who surrounded her bed, "You get away. Get out. Needles. Needles injecting something in my back. No! No! I don't want that, get away." As the third treatment was instituted, she showed impulsiveness, tried to strike the physician who stood by her bed, and made threats. "I'll hit you! Get away. No! No!" Then, showing a certain associative process of understanding, she added, "I don't want needles. I don't want to eat," together with many other remarks including profane and obscene words. At this third intervention the patient caused some consternation among those present when she explosively said, "No! No! Get away! No! No! I don't want to eat," and then using vulgar words added that eating was sexual intercourse and she did not want to do it.

This meant more to me and all the doctors present than the fact that she was eating. It made us realize that for a period of almost ten years Mary had not eaten and had never been approached by any stimulant to make her admit why she was not eating. For about ten years she was mechanically fed just because she did not want to submit herself to sexual intercourse. She lived all this time keeping this torturing secret within herself and without the opportunity to unload or ventilate through the influence of benevolent psychotherapy. The psychiatric approach in this case should essentially be credited to the use of sodium amylal, which is now used very extensively at the Northampton State Hospital principally for the treatment of catatonic phenomena.

I have very little time left to expose the check-up methods which I promised to describe in this paper in order to prove the evidence of the success of our work, and I shall simply mention a few figures which, in my opinion, are quite convincing:

A. Of the four other patients who were put on radical sodium amytal treatment at the same time as Mary, three showed immediate positive responses and began to eat almost as promptly as Mary did, kept it up with the aid of sodium amytal, and, according to my records, have from the 5th, 7th, and 8th day of initial treatment respectively taken an adequate and sufficient amount of solid food spontaneously and were never again fed otherwise. The fourth case, one of profound stupor diagnosed as Manic Depressive Psychosis, Stuporous type, showed more stubborn tendencies, failed to respond even to extensive doses for several days, and did not really begin to eat until the 17th day of treatment when she actually started to eat and has not been tube fed since. She is doing well at present.

B. From January 15 to April 14, 1938, fourteen new patients were admitted to our service with already well-established catatonic phenomena or in full-fledged stupor. Fearing that they would refuse to eat, we instituted prophylactic measures at once and gave these patients sodium amytal from 10 to 15 minutes before each meal for a few days. It would be difficult to state that we obtained 100% results as one cannot establish positive data on possibilities or probabilities, but I am proud to state that we aborted the necessity of tube feeding each and every one of these fourteen cases.

C. Far from being exclusively directed toward this particular manifestation of "refusal of food," the use of sodium amytal has also brought about remarkable results in the psycho-ventilation of all of the above-mentioned cases. Five of these fourteen patients, who happened to be my personal patients, were also mute upon admission. Under ordinary conditions I would probably have been forced to describe simply their facial expression, somatic reactions, etc., but through the administration of sodium amytal and interviews at auspicious moments, I was able to obtain some fragmentary statements from them which proved to be valuable clues toward psychotherapeutic "mise-en-scène." A thirty-year-old ex-supervisor of an important obstetrical clinic of a large town in the western part of Massachusetts, who had been mute and totally withdrawn from reality for several days, while under the influence of sodium amytal shouted at me, "I am pregnant. I am afraid! I must be pregnant." Not even her family physician, no one, had known her mental contents for weeks and this spontaneous explosion—another credit to sodium amytal—established a real foundation for psychotherapy.

I did not wish to bore you with statistics which would be very meagre at best. This paper is simply a humble contribution, an "expose" of my own experiments which turned out to be successful, but were not intended to be on a propagandary basis.

BIBLIOGRAPHY

1. Fischer, E. and von Mering, J.: Ueber eine neue Klasse von Schlafmitteln. *Therap. d. Gegenw.*, 5: 97-101, 1903.
2. Harris, Meyer M. and Katz, Siegfried E.: The effect of the administration of sodium amytal and sodium rhodanate on mental patients. *Am. Jour. Psychiat.*, 12: 1065-1083, 1932.
3. Bleckwenn, W. J.: Production of sleep and rest in psychotic cases. *Arch. Neurol. and Psychiat.*, 24: 365-372, (Aug.) 1930.
4. Bleckwenn, W. J.: Narcosis as therapy in neuropsychiatric conditions. *J.A.M.A.* 95: 1168-1171, (Oct.) 1930.
- Solomon, H. C. et al.: Some effects of the inhalation of carbon dioxide and oxygen, and of intravenous sodium amytal on certain neuropsychiatric conditions. *Am. Jour. Psychiat.*, 10: 761-769, (Mar.) 1931.
- Kläsi, J.: Ueber die therapeutische Anwendung der "Dauernarkose" mittels Somnifens bei Schizophrenen. *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 74: 557-592, 1922.
5. Foley, William H. and Rossignoli, Vincent P.: Sodium amytal as a substitute for tube feeding. *Am. Jour. Psychiat.*, 94: 639-641, (Nov.) 1937.

DISCUSSION

DR. SOLOMON: This paper of Dr. Longpre's is now open for discussion.—Will you please come forward?

DR. DANIEL J. SULLIVAN (*Boston State Hospital*): May I compliment Dr. Longpre on his very valuable paper describing his experiences with sodium amytal, which experiences I think have been of definite value to him and to the rest of us. Perhaps a general survey of the results of sodium amytal usage might be of interest. We have found that first, in the care of disturbed patients it reduces the amount of restraint in seclusion and the frequency of accidents and injuries to both patients and personnel. Secondly, we can take patients who are acutely disturbed, partially reduce their activity by proper amytal dosage, then put them on outdoor projects, or in the occupational therapy shop and tire them by physical work so that at night they do not need sedation to help them sleep. Thirdly, we also have found that it controls our tube-feeding cases since by giving them injections of sodium amytal at regular daily intervals we have been able to discontinue the majority of our tube-feeding cases. Fourthly, it helps to start retarded catatonic patients into activity; we give patients of this type a stimulating injection and as they react we take them to an occupational therapy class, or out for a walk, and get them interested in some group activity such as games or calisthenic exercises. Fifth, it gives us a method of "getting at" a new patient, as we often are able to stimulate a mute catatonic patient to talk and give us valuable information concerning his personal history and his individual difficulties; as a differential diagnostic point it is sometimes possible to differentiate between a catatonic stupor and a manic-depressive stupor on the basis of their type of reaction to a stimulating dose of sodium amytal intravenously.

The pharmacology or rather the psychopharmacology of the drug is quite interesting and most of it, I am afraid, is just theory. Sodium amytal may first be considered as a cortical depressant; when given in indicated dosage it overcomes the excessive inhibition of the catatonic patient, enabling him to give voice to his mental difficulties. Evidence of the cortical depressing influence of sodium amytal is shown by the occasional occurrence of increased knee jerks, ankle clonus, and positive Babinskis. There is also some effect upon the hypothalamus, which affects the metabolic centers, resulting in certain physiological changes such as dilatation of cerebral blood vessels, lowering of blood pressure, marked lowering of the oxygen consumption rate, a decrease in the oxygen and dextrose uptake by brain tissue, a change from abnormal to normal in certain neuro-muscular responses as measured by the chronaxy method, and the production of sleep.

What is the clinical psychiatric picture we see in a variety of cases given sodium amytal by injection? The essential changes are apparently the result of a removal of the censor. The mute schizophrenic talks, reveals his conflicts, describes his delusions and hallucinations, etc. The evasive or retarded schizophrenic who usually gives monosyllabic or cryptic answers to questions now talks readily and reveals conflicts underlying his attitude, delusions, and ideas of reference. The manic or hypomanic patient quiets down and gets blessed relief from the pressure of his psychomotor activity. The involuntal patient relaxes and gets a temporary peace from the torments of his former agitation, depression, or essential melancholy. The depressed patient may for the first time show optimism, and try to formulate plans for the future. These changes in the clinical picture of certain varieties of psychotic patients are unfortunately temporary but at the same time they are of definite value from both diagnostic and therapeutic standpoints.

Finally, in closing my remarks, may I make a plea for the more frequent use of sodium amytal? I think we have been side-tracked by so much insulin and metrazol. Insulin requires a rather complicated set-up and hours of observation; metrazol requires a brief injection period, followed by a short convulsive period, and then a period of observation; sodium amytal is readily given, requires no elaborate set-up or extraordinary precautions, and is usually a pleasant experience for the patient. With sodium amytal each man can handle his own cases efficiently and easily; the drug affords him a ready method with which to contact a variety of patients, particularly from the viewpoint of individual psychotherapy.

DR. SOLOMON: Is there any further discussion?

DR. R. G. HOSKINS (*Harvard Medical School*): Mention might be made of an idea which was brought to our attention by Dr. Quaestel of Cardiff, Wales. It appears that in Cardiff they have pushed sodium amytal considerably harder than has been the American custom. The difficulty in pushing it is that one gets toxic results after a time, but, according to Dr. Quaestel, by the adjuvant use of insulin and glucose, the toxic effects can be avoided.

DR. SOLOMON: Any further discussion?

DR. MORRIS YORSHIS (*Worcester State Hospital*): Apropos to what Dr. Hoskins said, Dr. Palmer reviewed the work on sodium amytal narcosis in the issue of the *Journal of Mental Science*, November, 1937, and he apparently does not corroborate Dr. Quaestel's remarks, indicating that with a control series of patients given sodium amytal or somnifen and another group receiving insulin and glucose in addition, the implications were not fewer than in those cases given sodium amytal alone.

DR. SOLOMON: Any further discussion? I might just add what you probably all know, that drugs like coramine are direct antagonists of sodium amytal, and if an overdose of sodium amytal is given, a patient can be brought out of narcosis very promptly by intravenous administration of coramine. Patients have been given as much as 30 to 40 to 50 and even 60 grains of sodium amytal intravenously and given 5 or 6 ampules of coramine and brought right out of deep stupors. Any further comments? If not, we'll turn to the next paper by Drs. Farrell and Vassaf of the Metropolitan State Hospital on "Insulin Therapy Supplemented by Psychotherapy."

DR. MALCOLM J. FARRELL (*Metropolitan State Hospital*): The subject is "Insulin Treatment and Psychotherapy in Chronic Dementia Praecox Cases."

INSULIN TREATMENT AND PSYCHOTHERAPY IN
CHRONIC DEMENTIA PRAECOX PATIENTS *

By MALCOLM J. FARRELL, M.D., and ETEM VASSAF, M.D.
Metropolitan State Hospital

Since Manfred Sakel introduced the insulin hypoglycemic shock treatment for dementia praecox, there appear to be varying opinions concerning its efficacy. In cases ill less than six months, Sakel (1) reported full remissions in 70 per cent, with improvement so that they could return home and carry on gainful occupations in an additional 18 per cent. Dussik and other European (2) investigators have essentially substantiated Sakel's high recovery rate. In the hands of American investigators, this method has not yielded the high remission rates reported from abroad. Cameron and Hoskins (3) believe that there is a higher proportion of unfavorable results among relatively small series, and they suggest that experience is an important factor. We feel that there are other important aspects of the treatment which are very often neglected or given scant attention. We refer to clinical procedures and the psychotherapeutic aspect of this treatment. It is the purpose of this paper to present our method of insulin shock treatment, giving particular attention first to clinical procedures, and secondly to the psychotherapy.

CASE MATERIAL

A total of five chronic cases from the female service were selected, the duration of illness ranging from five to twelve years. All cases showed the cardinal symptoms of dementia praecox, namely, hallucinations, loosely knit unsystematized delusions, incoherence, irrelevancy, blocking, mannerisms, seclusiveness, intrapsychic ataxia, lack of insight, and poor judgment with marked emotional and varying degrees of intellectual deterioration. All cases were presented at formal staff meetings, and a diagnosis of dementia praecox was unanimously made. Two patients were in the paranoid group and three in the hebephrenic group. Careful physical and laboratory examinations were made to rule out the presence of physical disease. The ages varied from twenty-five to thirty-nine years. No special criteria were used in the selection of the cases.

TECHNIC

A section of the Medical and Surgical Center was selected in which to carry out the treatment, inasmuch as it afforded a quiet, roomy, and adequate place where this group could be isolated from other patients. We feel that isolation from other mentally ill patients is extremely important from the standpoint of suggestibility.

The personnel was carefully selected, importance being placed on intelligence, tactfulness, attentiveness, interest in this particular field, courage, emotional stability, and sound judgment. There is little doubt that much of the success of treatment will depend on nursing assistance and care. This special group of employees remained permanently with the insulin group, having no other hospital duties. Special instruction was given to the personnel by the physicians in charge. Emphasis was placed on the nature of dementia praecox, the rationale of the treatment, the physiological and mental changes to be expected, nursing technic as applied to this treatment, danger signs, and reactions, together with a discussion of each individual case. It is felt that inadequately trained nurses may produce unfavorable mental reactions, and their failure to observe danger signs may result disastrously. Invariably the nurses felt and appreciated their important part in this treatment. About once a month during the course of the treatment a meeting of the entire personnel was held in order that each person could express his ideas, ask questions, offer suggestions, and discuss the changes, both mental and physical, noticed as the treatment progressed.

Extreme care was taken to make certain that all necessary equipment and medication were in a readily accessible position near the patients. Glucose, 35% solution, was kept ready for instant use in syringes. This medication was kept at body temperature with use of hot water bottles and blankets.

After searching physical check-ups, and about two weeks prior to the beginning of the treatment, the selected patients were transferred to the insulin ward in order to build up their physical condition. They were placed on a high carbohydrate diet, including some heavy meat, to supply protein, and fresh fruit, green vegetables, milk, and cod liver oil to supply vitamins. Weights were checked each morning at the same time, and temperature, pulse, respiration, and blood pressure were recorded twice a day.

The insulin treatment was carried out in a darkened, quiet room. Patients were given an enema early each morning. We feel that the enema is necessary as praecox

patients tend to have inadequate bowel movements. The presence of flatus or of a full colon might conceivably result in irritability or distress. The insulin was given daily, except Sundays, at 7:30 a.m. The initial dose was 10 units, this dosage being increased 5 units a day until the satisfactory shock dosage was obtained. This varied in our cases from 35 units in one to 265 units in another. All patients showed individually different reactions both mentally and physically.

The symptoms of hypoglycemic shock and danger signs have been adequately covered in numerous other papers and need not be repeated in this paper in detail. All of these patients showed a drop in body temperature, an occasional 94° axillary temperature being recorded. Efforts to maintain body temperature were made by supplying hot water bottles and heated blankets. From four to six hot water bottles were used for each case, the water being changed every half hour. Caution was taken to prevent burns. This procedure aided in producing the favorable so-called "wet shock." No unfavorable "dry shocks" were observed in our series.

If epileptiform convulsions occur in the course of the treatment, many authors have advised immediate termination of the treatment. That severe convulsions are a danger signal we readily grant. However, we have observed that following these severe reactions a definite improvement in the mental condition was noticed. For this reason, we have allowed our patients to continue in spite of relatively mild epileptiform convulsions. These mild convulsions were considered favorable provided they lasted no longer than from 30 to 40 seconds with an interval of one to two minutes between each. In one case fifty-three mild convulsions were recorded during one treatment with intervals between ranging from a few seconds to a few minutes. During this time the patient's general condition was carefully observed to make certain that she was in a satisfactory state. Shortly after, the patient went into a deep quiet coma. Much improvement was noted following these reactions. Among our five chronic patients two showed no convulsions. These patients have required high dosages and improvement in their mental condition has not kept pace with those patients who have shown convulsions. We therefore feel that mild convulsions are desirable provided the physical condition remains satisfactory.

An arbitrary time was set for termination in each case. This time was decided, taking into consideration the physical condition during the treatment and the mental reactions of the patient following termination of the treatment on the previous day. The length of treatment varied for each case, the average being, from 2½ to 3 hours from the time of injection, with coma lasting from 20 to 60 minutes. One case, however, was allowed to remain under treatment for 5 hours. We attempted to find the duration of treatment which will not result in tiredness, irritability, and confusion.

Termination was accomplished whenever possible by the use of the nasal tube. Occasionally a patient did not arouse in a satisfactory manner within 15 minutes. In these cases supplementary intravenous injections of glucose were given. In two cases nasal feedings were not possible; therefore intravenous injections were used. On arousal an ice cap was applied to the head and the face was sponged with cold cloths. We feel that these procedures were stimulating and aided in reducing cerebral congestion and irritation. The patient remained in a flat position for at least ten minutes following arousal, after which the head of the bed was slightly raised. This care was taken in order to prevent cerebral anemia. This caution should be especially followed when patients receive high doses of insulin. Dry bed linen was then supplied, and a light breakfast, consisting usually of grapefruit, sugared milk, and toast with jam, was given. This small meal was taken in bed and usually would carry the patient until the high carbohydrate dinner was served. After a half-hour period of rest, a lukewarm shower was given and the patient allowed to dress. During this entire procedure the physician remained on the insulin ward, not leaving until he was satisfied that the condition of the patient was satisfactory and that the patient was eating her dinner in a proper manner. During the period from termination on, the physician must be prepared to combat secondary reactions. Mild reactions such as paleness, cold and clammy sweating, changes in pulse rate and quality, mild euphoria, and sudden assaultiveness, usually indicate a secondary hypoglycemic state and may be combated by returning the patient to bed and administering sugar by mouth. Nausea and vomiting must be combated with intravenous glucose, usually 100 cc of 35 per cent glucose being

sufficient. The severe secondary reactions, such as twitchings, semi-comatose state, and coma, required immediate intravenous glucose. Occasionally signs and symptoms of circulatory collapse were noted. Patients showing this condition were put to bed at once, hot water bottles and heated blankets being applied. Stimulation was given whenever indicated.

In spite of such a rigorous treatment all patients showed marked improvement in their physical condition. Gains in weight during two months were noted in all cases and varied from seventeen to twenty-eight pounds. Normal menstrual periods were resumed in one patient who showed amenorrhea for over a year. Another patient became quiet during her periods, whereas previously she had been disturbed, assaultive, and destructive during those times. These observations might indicate some favorable readjustment of the endocrine system. Moderately severe acne vulgaris showed improvement almost at once in two cases. The appetite in all cases became much better. Low blood pressure was noticed in all cases prior to the treatment; during the course of the treatment it improved considerably, rises being noted of from twenty to thirty points, indicating a much improved circulation.

It is our conviction that psychotherapy must be used in conjunction with the insulin treatment in order to obtain the desired results. In this treatment, psychotherapy differs from the ordinary type, no attempt being made to uncover hidden conflicts that may account for the abnormal behavior. Such probing into painful experiences may be dangerous, inasmuch as these people appear to be in a sensitive and suggestible mental state as a result of the treatment. Psychotherapy in our hands has consisted mainly of suggestion and re-education. We feel that it is very important for the physician to remain at the bedside, not only to cope with emergencies that may arise, but to gain a better insight into the patient's mental state. It was observed that on many occasions, while the patients were in the drowsy state, they gave valuable hints concerning hidden conflicts. After termination, these patients often reported dreams, many of which gave information which aided in understanding some of the patient's difficulties.

Suggestion can be used at any time during the day. Opportunities constantly present themselves to the alert physician to offer suggestions intended to encourage more normal types of behavior. However, we feel that these patients are in the most favorable state to receive strong suggestions during the drowsy period just prior to coma and the drowsy period immediately following termination. During these periods the patients are usually relaxed and inhibitions are removed, thereby rendering the patients more vulnerable to such an approach. In many respects these periods may be compared to an hypnotic state. As a corollary to this idea, extreme caution was observed in conversation between personnel during those stages in the course of the treatment. Any reference to the physical state, such as condition of the pulse, temperature, or unusual signs or symptoms, might result in fright, which in turn might serve as a basis for persecutory ideas. Our suggestions ignored past behavior but were centered about developing proper attitudes toward the future. A point may be reached where the patient is very resistive toward a particular suggestion. In this condition we did not become insistent but changed the subject or waited for another opportunity. Eventually these patients may become inquisitive about their own condition, about the treatment, and about their environment. If these questions are directed toward the nurse, she will not answer herself but reassure the patient and refer the questions to the physician for reply. Needless to say, when such a patient asks these questions, improvement may be considered to have taken place. All replies must be carefully planned or else severe psychic shock may be the result. We have found that replies referring to the necessity of physical improvement, such as gain in weight or the need for rest, usually were satisfactory. No reference to mental illnesses was made. To this end the patients were denied visitors until such time as they requested to see their relatives. All visitors were interviewed by the physician. Definite instructions were given, including the request not to discuss the mental condition or the treatment with the patient. The conversation offered by relatives was to be centered about how well the patient appeared and generalities about the home, other relatives, the weather, and topics of current interest. Many times a point is reached where the patient begins to wonder or ask questions about the treatment. This is a critical

time and must be handled carefully by the physician. The injections, the darkening of the room, the various routines of treatment suggest to the patient that there is something wrong with her so that treatment is required. This autosuggestion is a valuable aid in the development of insight. Many times the patients reported dreams that were frightening to them. Often they would cry when reporting them or repeat such phrases as "God help me", "Help, mercy", "I'm going crazy", "I think I'm crazy." At least they are stirred out of their self-satisfied, self-sufficient state even if only for a short period.

Re-education has a prominent and important place in our treatment. We use the word re-education advisedly, since the dementia praecox patient has not forgotten what he has learned but rather he has become disinterested in it. As soon after termination as the patient's condition warranted it, she was encouraged to help with light tasks about the ward. These tasks were very simple at first and were then made increasingly complex, as the mental condition warranted it. At the dinner table particular attention was paid to the serving of meals in an attractive manner. Table manners were given special attention and faulty manners were discouraged. Following a short period of rest after dinner, the group went to an Occupational Therapy Center accompanied by a nurse who could observe any danger symptoms that might suggest an incipient secondary reaction. One occupational therapist was assigned to this group and she remained in attendance throughout the course of the treatment. No other patients occupied the room at that time. Classes were held daily for one and a half hour periods. Patients were observed closely, and carefully selected activities, adapted to the needs of each individual, were used. Through crafts, an attempt was made to improve attention and concentration, replace indifference by interest, substitute activity for inactivity, and replace day-dreaming by sustained effort. Parties, games, and reading aloud were used as socializing agents, in order to interest the patient in others. Interest in personal appearance was encouraged by dressmaking. In this connection the hairdresser made frequent visits to the ward to give attention to hair and fingernails. Shorthand, typewriting, and music were used in an effort to re-establish capacity for social usefulness. In short, we attempted to find something constructive yet satisfying for each individual.

After the occupational therapy class was concluded, and weather permitting, the patients were taken for walks about the hospital grounds. Interest in plants, flowers, and birds was stimulated. On other days, this group was taken to the Recreational Center, where they were instructed and encouraged to participate in the various games, such as bowling, ping pong, and pitching horseshoes. It is interesting to note that the skill demonstrated by some of these patients who had not played any games for from six to twelve years was truly remarkable. As a result of these trips and games, it was not long before some of the patients stated that they would like to go for a ride or to go home. Accordingly, short auto rides, shopping trips, and finally visits to their homes were arranged with their relatives. Usually a nurse accompanied the patient on the first trip to make certain that the relatives understood the patient and that they carried out the physician's instructions, and to observe and report to the physician about the patient's behavior. As the mental condition improved, the visits at home were lengthened. This was done in order to aid social readjustment. Whenever the patient remained out of the hospital overnight, the relatives contacted the physician by telephone, giving reports about the patient's behavior. The patient was encouraged to help with light housekeeping, and interest in current events was stimulated. Relatives and old friends were invited to the home and return visits arranged. Auto rides and shopping trips were taken during which the patient was given every opportunity and encouraged to make decisions or suggestions. From time to time the physician talked with the patient by telephone. In this manner close contact between physician and patient was maintained. In those patients who remained at home improvement continued each day. It should be pointed out that when a patient was in sufficiently good mental condition to leave the hospital her case was not presented at a formal staff meeting. Her mental condition was discussed with other staff members who could interview the patient singly or in pairs on the ward so as to satisfy themselves as to patient's mental status. We feel that the embarrassment or other mental reactions resulting from the patient's appearing before such a

meeting would have a decidedly poor effect on the patient. These patients suffer from a marked inferiority feeling to begin with and the usual formal staff meeting may only accentuate that feeling.

RESULTS

Early in the treatment all patients showed improvement in eating habits; actions became more free and unconstrained; more interest in the environment was noticed, and most of the patients inquired for relatives. Disturbed and destructive patients became quiet and more amenable to supervision and treatment. All persons who had not seen the patients except prior to the start of the treatment were amazed at the change in facial expression: expressions almost devoid of emotion appeared to be replaced by a more normal appearance. The emotional rigidity, a cardinal symptom of dementia praecox, appeared as if limbered up and replaced by psychomotor symptoms of better contact with environment. Following visits with relatives, all patients displayed emotion both on arrival and departure; most of these patients showed little or no emotion under similar circumstances prior to the treatment. As the patients improved, they expressed interest in other patients in the group, more sociable behavior being very prominent.

In these chronic patients, the more favorable results appeared in the younger age groups and these younger patients required smaller doses of insulin to produce satisfactory shock.

The condition of our five chronic patients at the end of three and a half months of treatment shows that one patient is markedly improved and is at home on indefinite visit, another is improved and is allowed out of the hospital for short visits at home, a third is slightly improved and has been allowed out overnight, while the remaining two cases show little if any improvement.

We fully recognize that this report is based on a relatively small number of cases; however, we feel that our results indicate that further use of this treatment is desirable.

CONCLUSIONS

1. Insulin shock treatment of chronic dementia praecox, when combined with psychotherapy, is a promising method of treatment.
2. Complete isolation of the patients under treatment from other mental patients is essential.
3. Mild epileptiform convulsions when properly handled are valuable assets during the course of the treatment.
4. Adequate instruction should be given to personnel prior to treatment.
5. Adequate diets, rich in vitamins, are desirable.
6. Careful supervision and observation must be given during the entire treatment.
7. This treatment is dangerous, but courage, hopefulness, and good judgment are necessary on the part of the physician.

BIBLIOGRAPHY

1. Sakel, Manfred: Schizophreniebehandlung mittels Insulin Hypoglykämie sowie hypoglykämischer Schocks. *Wien. med. Wchnschr.* 84: 1211 (Nov. 3), 1265 (Nov. 17), 1299 (Nov. 24), 1326 (Dec. 1), 1353 (Dec. 8), 1383 (Dec. 15), 1401 (Dec. 22) 1934; 85: 35 (Jan. 5), 68 (Jan. 12), 94 (Jan. 19), 121 (Jan. 26), 152 (Feb. 2), 179 (Feb. 9) 1935.
2. Dussik, K. T. and Sakel, Manfred: Ergebnisse der Hypoglykämie-shockbehandlung der Schizophrenie, *Ztschr. f. d. ges. Neurol. u. Psychiat.* 155: 351-415, 1936.
Müller, cited by Glueck, Bernard: Hypoglycemic state in the treatment of schizophrenia. *J. A. M. A.* 107: 1029-1031 (Sept. 26) 1936.
Benedek, Ladislaus: Insulin-Schock-Wirkung auf die Wahrnehmung, Berlin, S. Karger, 1935.
Berglas, B. and Süsić, Z.: Ueber die Hypoglykämie-Chokbehandlung der Schizophrenie, *Psychiat.-neurol. Wchnschr.* 38: 599-602 (Nov. 28) 1936.
3. Cameron, D. E. and Hoskins, R. G.: Experiences in the insulin-hypoglycemia treatment of schizophrenia. *J. A. M. A.* 109: 1246-1249, (Oct. 16) 1937.

DR. SOLOMON: This opens up the subject in which I suppose everybody here is vitally interested. I'd like to call attention to one thing that is brought out very clearly in this paper. One constantly hears families of patients ask, "What is it that the state hospital has to offer? What does treatment consist of?" I think here has been a very pretty illustration of what can be done, what can be related to the relatives as to what is done for patients in a hospital where one is thinking and acting for patients. It is a pretty illustration of what psychotherapy may be in a hospital where it is not a matter of an hour's interview per day, but where a scheme for living and activity is worked out. This paper is now ready for discussion. Who will say a few words?

DR. E. PHILIP FREEDMAN (*Northampton State Hospital*): First let me express my admiration for Dr. Farrell and Dr. Vassaf for their careful and scientific exposition. From the paper by Sakel which appeared in the January, 1937 issue of the *American Journal of Psychiatry* the following is quoted: "Though it is clear that the shock plays a conspicuous rôle in the therapy, the main factor appears to be the hypoglycemic state. It has long been known that a shock may relieve a mental disease. It is also known that severe illness may for a time favorably influence a case of schizophrenia. All these effects, however, are transitory. It is my belief that the effectiveness of the hypoglycemic insulin treatment is due to the action of the insulin directly on the cell itself." Now using the above as a premise, I determined to experiment on a limited number of patients. My aim was to determine whether any improvement in the mental status could be obtained without the hazard of severe hypoglycemia and shock. There were 12 patients. The dosage varied in the beginning from 6 units t. i. d., later 10, and then 15 units t. i. d. The results were as follows: B. F., a mute and seclusive patient of more than four years' duration, began to talk, danced in the hall, and mingled with the others to a limited extent. However, active tuberculosis set in and after a short time the patient died. C. H., prior to treatment was hallucinating freely and was quarrelsome. She began to improve, claimed she no longer was hallucinated. Her relatives claimed she gave up all of her silly delusions. It is now more than 10 months since she went on visit. A. R. on July 5th weighed 91½ pounds, on November 5th, 110 pounds; Is now on visit, fully recovered. M. H., weighed 127½ pounds. Coincidental with increase in weight there was improvement in the mental condition, and when she reached 165 pounds treatment was discontinued and trial visits were recommended. However, three weeks after discontinuing treatment the patient relapsed and her condition became as bad as it was two years ago. Considering the remaining cases, when subjected to careful examination, some transient improvement may be noted. Practically all have been transferred to our metrazol clinic and those who have received metrazol have shown improvement, all easily demonstrable—some markedly and dramatically. Therefore, considering results, it seems to me that the administration of insulin without shock does not compare unfavorably to that of insulin with shock. If we consider the time spent with each patient, the special arrangements made—including the precautionary measures, etc., I cannot help feeling skeptical as to the advisability of such heroic measures, at least when based on the results obtained by Dr. Farrell's efforts. The prompt and in some cases almost miraculous response with metrazol is so dramatic that the results of insulin, when compared with metrazol, seem to fade into the background. Apropos of the section of the paper dealing with psychotherapy—obviously there can be no quarrel, though I cannot say that I would incorporate all the restrictive measures. I feel that psychotherapy is an important part of any form of treatment. The fundamental weakness of both paper and discussion lies in the limited number of cases. In one sense past and continued efforts in insulin therapy as well as metrazol are justifiable, because they are an indication that therapy in psychiatry—to paraphrase a well-known and illustrious citizen of the United States—is on the way.

DR. ETEM VASSAF (*Metropolitan State Hospital*): I want to thank Dr. Freedman for his interest in and discussion of our work. As you all know, insulin treatment differs a great deal from metrazol treatment. However, so far as our work in insulin treatment is concerned, I believe we are not losing any time. It seems

hardly worthwhile to work with only a few patients in a few hours' time because we like to look for very good results in dealing with schizophrenic patients, possibly in one month, or possibly in six months. We combine psychotherapy with our insulin treatment and we are getting very good results. We are not having any relapses, whereas in metrazol treatment, according to the literature as well as my own personal experience with this form of treatment, there have been relapses. In insulin treatment we can handle the patients very carefully and apparently without any damage or fatality. I've been associated with the work of insulin treatment for about two and a half years, this work comprising a series of about two hundred cases, and fortunately we had no fatalities. On the contrary, we have had from sixty-five to seventy-five per cent good results. The few cases reported today are chronic cases of long standing, rather than the early cases, and we all know there is a difference between the chronic case and the early case from the point of view of results. Among our patients, the duration of the illness averaged twelve years and their ages varied between twenty-five and thirty-nine.

Insulin Therapy			Age	Days of Rx.	Rest Days	Off Days	Units of Insulin	Shocks	Days of Convulsions	Rx. without Shock	Hypersensitism	Secondary Shocks	Gain in Weight	Condition at time of Rx.
January 19—April 30 1938														
Case No. 1.	.	.	36	64	14	20	4,505	31	3	33	1	0	24 lb.	†
Case No. 2.	.	.	25	77	14	10	3,655	45	2	32	2	1	20 lb.	†
Case No. 3.	.	.	39	60	14	24	2,220	46	16	14	2	0	20 lb.	†
Case No. 4.	.	.	37	80	14	7	5,675	51	1	29	4	0	20 lb.	0
Case No. 5.	.	.	37	76	14	10	7,795	41	1	35	8	2	17 lb.	0
Total							23,850							
Markedly Improved														
Improved														
Slightly Improved														
No Change														

In some cases we have given as much as over 7,000 units in spite of which the results were not as marked as in those cases who received much less insulin. Some of the patients who received large doses showed some sort of hyperinsulinism and secondary shock, following which they were very tired and required a rest period, the insulin treatment to be continued on those patients at a later date. I prefer the insulin treatment to metrazol treatment because of the slower effect of the former and also because I have more time to give psychotherapy. In metrazol treatment the patients develop a fear complex which I feel will do more harm *per se* than the good that may come from the metrazol. In metrazol treatment there are often relapses, and it is sometimes necessary to repeat the treatment every six months in order to get results. We believe that better results can be obtained where psychotherapy is given along with insulin treatment, and we suggest doing some sort of psychotherapy for metrazol treatment, principally because we are dealing with mentally ill patients, primarily, with whom psychotherapy is an important part of the treatment. It is true that insulin treatment requires more time than metrazol, but I think the results obtained from insulin are far more satisfactory.

I will repeat again, one must be very careful and have a great deal of patience and courage to give insulin treatment.

DR. D. E. EWEN CAMERON (*Worcester State Hospital*): I would like to congratulate Dr. Farrell on his excellent presentation of the place of psychotherapy in insulin treatment. I thoroughly agree with his point of view. It is sometimes very difficult, however, to carry it through as satisfactorily as one would like. The difficulties that come up are sometimes rather unforeseen. An instance of that is afforded by a patient we were working with about a year ago. He was making pretty good progress and, as a matter of fact, had got so far that we were able to give him parole. While out on parole one day on the grounds he met an attendant, or rather an ex-attendant who had been discharged for alcoholic indulgence. He was coming up the avenue to say goodbye to some of his friends and he was still

following his pastime and consequently was somewhat inebriated. He met the patient and said, "John, I'm glad to see you looking so well." The patient was rather pleased, but the attendant went on to say, "I imagine, however, that you won't be home more than a few days before you cut your — throat just like all you — patients do." The patient was very much upset by that and went into an anxiety state with physical symptoms, vomiting, etc. His symptoms returned in full force. We were able to overcome that by reassurance, and after a few more weeks of treatment he seemed fairly well and went home. He had been very anxious to go home and felt that whatever residuals remained would disappear as soon as he got into his own home again and the familiarity of his daily routine. However, he found that he just couldn't fit, things didn't go as smoothly as he had anticipated. He became very much depressed and worried, and made a suicidal attempt. However, further treatment and further explanation of his difficulties to him resulted in a very good adjustment and allowed him finally to go home and hold a rather responsible federal position.

Another example of need of careful individual supervision is afforded by a patient who is at present under treatment. This man has been suspicious of his wife for many years. He had for some weeks prior to treatment been seeing visions of her misconduct and also some very bizarre visions from the early history of the world. After he came in here and before treatment, he started to keep a diary, and we thought it would be interesting to allow him to keep this diary and see if it corresponded with any change in his mental condition. Unfortunately it became apparent that the keeping of this diary served to rather perpetuate in his mind his delusional notions. He became very fixed and definite in the idea that he could see these visions and that they meant something to him. We rather arbitrarily took it away from him and suggested that he might be interested in drawing, and provided material for him to make sketches. We pushed occupational therapy and work with the outside group, but nonetheless for two weeks there was a very definite relapse. This has now subsided under continued treatment and he is showing every evidence of making eventually an excellent recovery, but I think it is interesting to note that those things that he was recording in his diary have remained as residuals, and we are still trying to eliminate them by further treatment.

These examples illustrate the very large range of effort which is required and which is comprised, to our mind, under the term psychotherapy.

DR. SOLOMON: Any further discussion? Now if you'll turn to the next paper on "The Significance of Behavior during Hypoglycemia," by Dr. Wall.

SIGNIFICANCE OF BEHAVIOR DURING HYPOGLYCEMIA

An Abstract

BY CONRAD WALL, M.D.
Worcester State Hospital

It has been observed by Sakel and others that a given schizophrenic undergoing insulin therapy is apt to show an individual pattern of behavior which is repeated on successive days of treatment. Thus one patient will continuously bite at the bedclothes, another will repeatedly make sucking movements and another will make diffuse, apparently purposeless movements. This characteristic individual pattern can be observed in both the hypoglycemic and emerging states.

In my own observation of patients under treatment, it became evident that at least some of them were showing a progressive change in behavior pattern. The question arose as to possible meaning of such change and its connection, if any with the change in the mental state.

In order to collect information upon this point, observations on the behavior of each patient during the course of treatment were recorded by the nurses and physicians. This behavior falls best into two classes of movement and verbal productions. The two classes of movement are: first, restless thrashing about without any apparent purpose; second, specific actions such as sucking, biting, rhythmic movements of the limbs, getting out of bed, etc.

For illustration of behavior during the hypoglycemic state, the following four cases were reported.

1. M. R. A 19-year old unmarried girl with diagnosis of Schizophrenia, Mixed Catatonic and Paranoid Type.

During hypoglycemia, this patient showed in the first period sucking and biting movements. In a second period, masturbation was an outstanding feature, and in the final phase of treatment coital movements appeared. Parallel with this succession of behavior, there was a rapid improvement in the patient's condition. At present, she is in a good state of remission.

2. M. V. A 20-year old unmarried girl, with a diagnosis of Schizophrenia, Catatonic Type.

In this case, the specific acts during hypoglycemia consisted of sucking movements. Masturbation and coitus-like movements were not present. There was, however, a marked change toward heterosexual interests which clearly appeared in fragmentary verbal productions and hallucinations in the hypoglycemic state as well as in her overt behavior when emerging from coma.

3. H. D. An 18-year old girl with a diagnosis of Schizophrenia, Hebephrenic Type.

She showed sucking and biting early and throughout treatment. After three months of treatment with no change in condition, rhythmic friction of thighs appears, followed by coital pelvic movements with an increased interest in the opposite sex upon emerging. This was accompanied by a change for the better. During the remaining period of treatment this physical phenomena did not recur nor was there any further improvement in the patient's mental condition.

4. E. M. A married woman of 32, diagnosed Schizophrenia, Catatonic Type.

During the first period of treatment, she masturbated in hypoglycemia and showed improvement. During a subsequent period of quiet coma, her clinical condition was stationary. In a third period, masturbation reappeared, accompanied by a dream of coitus on one occasion. This period was associated with further improvement. In a final period, she showed no sexual behavior but was diffusely overactive and became worse.

It did not seem wise to make generalizations from such a small amount of material. It did seem, however, that there were certain cases which showed progression from sucking and biting to sexual movements while undergoing insulin treatment. It further appeared that when oral movements predominated there was no improvement and that with the occurrence of sexual movements or heterosexual interests, improvement did occur.

The implications of the above-described phenomena in terms of the psychoanalytic theory of regression are fairly evident. Further observation will be necessary to establish the constancy and generality of the described behavior in association with clinical status.

DISCUSSION

DR. SOLOMON: Dr. Farrell, do you want to start the discussion?

DR. MALCOLM J. FARRELL (*Metropolitan State Hospital*): I think Dr. Wall is to be complimented certainly on his very interesting paper and his method of presenting it. It is particularly interesting to us that Dr. Wall finds that the stage just before coma is an important one. We quite agree with that, as you have probably noticed from our paper. Improvement as a result of the insulin shock treatment perhaps may be grouped in two parts, physiological and mental. I feel a little at a disadvantage to attempt to discuss this because our cases have all been chronic ones. However, schizophrenics for the most part seem to show a diminution in sex functions, although there are a few, of course, that do show an increase. Whatever the reason is we don't know, although there have been several suggestions. Perhaps endocrine imbalance, or perhaps, as Dr. Gellhorn states in a paper published recently, I think in the April 30, 1938, issue of the Journal of the American Medical Association, wherein he feels that the stimulation of the sympathetic system is at the basis of improvement. We rather feel that perhaps the endocrine imbalance may be the answer, and that insulin does produce a favorable readjustment. Some of our cases have not shown the reaction Dr. Wall speaks of. Two of the five did; one showed no improvement and one showed slight improvement. There again I recognize that the length of illness may be quite important. One or two other findings might be grouped in a narcissistic grouping. It seemed that very shortly after treatment was started, some of these patients showed a considerable interest in themselves, particularly in their appearance, and were especially pleased with hairdressing and with new clothing. Of course Dr. Wall's suggestion fits in quite well with the Freudian concepts of adequate emotional release and expression of conflicts which usually may be followed by improvement. I wonder if the time at which these expressions are given isn't rather important, particularly under insulin; it seems as though it comes at a time when the person would be least affected by the bringing up of painful experiences and painful conflicts, again during that period which we felt was important. Just one question occurs to me, and that is if Dr. Wall feels that sex conflicts are the major conflicts responsible for the difficulty, or whether he is considering only one aspect of some of the causes of dementia praecox.

DR. SOLOMON: Dr. Clark, do you wish to discuss this?

DR. CLARK: I think I have nothing to add.

DR. SOLOMON: Is there any further discussion? I think Dr. Wall has been very conservative in not attempting to draw too many conclusions, but presenting merely his findings and letting the rest of us adduce whatever conclusions therefrom we wish. Dr. Campbell, could you add anything to Dr. Wall's presentation?

DR. C. MACFIE CAMPBELL (*Boston Psychopathic Hospital*): Dr. Clark has had more immediate contact with the patients than I have and my observations have been somewhat fragmentary, supplemented by contact with the literature. As to the actual phases of the behavior observed during hypoglycemia and their significance as presented by Sakel and others, I must say that personally I do not feel that they are very convincing. With a complicated picture of behavior rapidly changing, it is difficult to state exactly the details and the significance of the complicated series of reactions. In the presentation by Dr. Wall I think it is interesting that we have patterns which are rather definite and clear-cut and can be correlated with various stages of maturity. These patterns may be interpreted in this genetic way, but the interpretation may be because they have been unduly isolated from the complex setting in which they occur. These are topics for additional observation and discussion and analysis. I think the lines along which these observations have been made are extremely important. From the point of view of methods it is of interest to observe that in the Illinois work where they are carrying on this treatment with a great deal of industry, the nurses have come themselves to the conclusion that there is a great deal of danger in making interpretations instead of objective observations; they have accordingly developed a rather rigid technique of observation.

DR. SOLOMON: Any further remarks? I take it that we are not going to ask Dr. Wall to answer Dr. Farrell's question as to the causes of dementia praecox, as that will open up something other than the pure therapeutic side of the project. I will now call on Dr. Michelson to read on the use of metrazol.

THE USE OF METRAZOL IN THE TREATMENT OF SCHIZOPHRENIA

BY HARRY MICHELSON, M.D.
Northampton State Hospital

Assuming that there is a biological antagonism between schizophrenic processes and epilepsy, Ladislaus von Meduna 1, 4, in 1935 introduced the treatment of schizophrenic patients by the provocation of convulsive seizures by metrazol or cardiazol. This drug has been, and is still, used in Europe as a cardiac stimulant in small doses administered mostly intramuscularly or subcutaneously. In mental hospitals this drug has been used with excellent results in paralytics subjected to malaria treatment during the post-febrile circulatory disturbances, and also in patients receiving a narcosis therapy, because of its beneficial effect on the blood pressure and respiration. The drug is a pentamethylenetetrazol. It is a crystalline powder soluble in water, quickly absorbed and eliminated. It is worthwhile mentioning that the composition of the drug is not affected by the sterilization process, and according to Rietschel, decomposition occurs only after heating to over 250° C. for several hours in an acid solution.

Referring to the anthropometric investigations of Graf, Delbruck, Kreyenbruck, and others, Meduna established his working hypothesis of the biological antagonism between schizophrenia and epilepsy on the following factors: First, both diseases are mostly associated with different constitutional bodily types. On the one hand, there is a predominance of the athletic and dysplastic types in epilepsy, while on the other, the usual type found in schizophrenia is that of the asthenic-leptosomic constitution. In other words, while the mesodermal elements are poorly developed in the schizophrenic, they are well formed in the epileptic habitus. Second, and this seems to be the fundamental basis for his working hypothesis, he points to the publications of G. Muller in 1930, Glaus in 1931, and Steiner and Straus in 1932, who emphasize the rarity of the combination of schizophrenia with epilepsy. In 1929 Nyiro found that of 176 epileptics only one per cent recovered spontaneously, but in cases where a schizophrenia developed in addition to the epilepsy, in 16 per cent the convulsions became rare and ceased altogether, and vice versa, the course of a schizophrenic process was favorably influenced by spontaneously occurring epileptic seizures. Indeed, we are able to report a case in our hospital which would confirm Meduna's conception of this antagonism. This patient has been a resident in our hospital for the past nine years and displayed very definite hebephrenic symptoms with catatonic coloring throughout his stay here, such as evasiveness, withdrawal from reality, facial grimacing, fixity of gaze, extrasensory perceptions, tendency to stereotypy and neologisms, which were the most prominent features in his case. He also showed vasomotor phenomena usually seen in catatonics. He was disturbed, noisy, and untidy and had to be kept on the more closely supervised wards. A year ago, that is, eight years after his admission, he suddenly suffered a convulsion which was followed by confusion and resistiveness. After this first convulsion the patient showed some improvement in his mental condition, was more alert, sociable, showed more spontaneity and a rather normal affect. In the course of the following months he suffered seven more epileptiform convulsions. At the present time he does not show any psychotic manifestations, has good insight into his condition, and will be discharged in the near future. Repeated physical examinations did not reveal any findings which would indicate an organic brain lesion or any other basis for these epileptiform seizures. This case is reported at some length because it is believed to be of rare occurrence. Furthermore, similar cases may be found in this and other hospitals. A group of such cases collected and analyzed from this point of view would be of distinct interest. Nevertheless, I believe that Meduna's hypothesis has not yet been proved. As a matter of fact, Low and his co-workers (6) look up all references at the Psychiatric Institute of the Research and Educational Hospital of the Illinois College of Medicine report in the April edition of the Archives of Psychiatry and Neurology good results even in the affective group of psychoses.

Encouraged by the favorable results reported, more and more institutions have introduced the irritative treatment, and as a result, the number of statistical and clinical reports is increasing. Since January, 1938 we have established in collaboration with Dr. Shapiro a regular Metrazol Clinic on the male and female wards as part of our routine work. Before the patients are subjected to this treatment, thorough physical and laboratory examinations, including blood sugar, N. P. N., urinalysis, and blood count, are performed. In some cases a fluoroscopy of the chest is made, and as far as the patients are coöperative, the basal metabolic rate is also determined. Every case is presented at staff meeting for diagnosis. Permission from the patient's nearest relatives, who are informed of the possible

complications, is obtained. In general, we did not have any difficulties in obtaining the consent of the relatives. As a contraindication for the treatment we regard cardiovascular and pulmonary diseases, acute or chronic infectious diseases, and organic changes in the central nervous system. The claim of some authors that the menstrual period is a contraindication for the treatment cannot be substantiated. We have treated patients regardless of their menstruation and were not able to record any ill effects.

The technique is a very simple one and consists in a rapid intravenous injection of 10 per cent metrazol solution. Although von Meduna regarded 0.5 gm. or 5 c.c. of the 10 per cent solution as the starting dose, we were able to provoke a convulsive seizure with 3 c.c. in the majority of cases. In one case a convulsion was produced with 2 c.c. We would like to emphasize that the rapidity of the injection is of extreme importance in the provocation of a seizure. We obtained the optimum results by injecting 1 c.c. in one second, but in some patients even this rapidity did not have the desired effect. By using the same amount in a shorter period of time—a half second per c.c., the patient suffered a full paroxysm. Apparently the determining factor is the momentary concentration in the blood, not the absolute amount of the drug. We were not able to establish a relationship between body weight and the amount of metrazol necessary for the provocation of a seizure, but we have to confirm the findings of Meduna, Finkelman, etc., that the dose had to be increased more frequently in an advanced psychosis of long duration than in cases of recent onset. In cases in which we succeeded in provoking a convulsion, the same dose was used for the second and eventually for the third time. In case of failure the dose was increased by one-half or one c.c. The highest dose used was 9 c.c. Recently we have been repeating the injection with a higher dose five or ten minutes after the first unsuccessful injection without any ill effects. The total number of injections in the completed cases ranged from 8 to 26. In accordance with other authors we determined that those patients who had the higher percentage of convulsive seizures in the series of injections showed better results than those with other incomplete reactions, such as aura, furor, confusion, etc. Not only because of the better results in those cases in which a convulsion resulted, but also from the psychological and human point of view, I think that it is of value to administer a full effective dose since patients who suffered a furor or a panic state with more or less sustained consciousness feared the treatment more than those who had a complete amnesia for the convulsion.

The psychotherapeutic factor during and after the metrazol treatment plays an important rôle. As soon as the patient shows some signs of improvement and some degree of rapport can be established, extensive psychotherapeutic measures should be instituted by encouragement, explanation, ventilation of the patient's difficulties, re-education by constructive occupational and recreational therapy, and eventually by short visits at home which give him more self-confidence and self-assurance. Therefore, we prefer to give the treatment three times a week instead of daily because we are able to give the patient the benefit of psychotherapeutic measures in the intervals. It is frequently striking to observe how the patients gain more and more insight into their condition, how they begin to show more interest in their surroundings, and how extrasensory perceptions and delusional ideas retreat into the background and gradually disappear. They begin to realize that the treatment is of benefit to them and acknowledge the efforts of the physician. We frequently transfer the patients to quiet wards and eventually give them parole privileges. It is remarkable that the majority of the patients gain considerably in weight during the treatment.

Concerning the motor patterns of the metrazol paroxysms, very valuable clinical observations were made by Finkelman and his co-workers (3) in the Elgin State Hospital with the aid of cinematographic and kymographic tracings. Also, Low and his co-workers (6) at the Psychiatric Institute of the University of Illinois College of Medicine recently published very interesting observations on this subject. In general, one can say that the convulsion in every phase shows a distinct, individual pattern. Slow motion pictures can and will give us further valuable information about the course of the paroxysms. The slightest reaction to the injection is an aura, which is either the only manifestation or the forerunner of the convulsive phase. The aura is dominated by subjective symptoms of a sensory nature. Patients describe their sensation as being unable to think, having a feeling of being narcotized, while some are only able to say that they have some kind of a "funny feeling" in

their heads. Others say that they see sparks or stars before their eyes, or have a "floating feeling." One of our patients sat up suddenly and stated, "Doctor, I am going to lose my mind." A severer prearoxysmal reaction is a furor or panic state with confusion, restlessness, fearfulness, and shocked facial expression. One of our patients had reactions of this kind, which lasted for about half an hour. During this state some patients may show slight twitchings of muscled, particularly those of the face. The major convulsion is frequently preceded by a short cough. After an interval of 5 to 10 seconds (recorded by a stopwatch), there develops a short clonic convulsion of from 3 to 10 seconds, which is followed by a tonic phase, the duration of which is about 5 to 30 seconds. The whole convulsion lasts for about 30 to 70 seconds. Shortly before the end of the seizure, the patient shows a marked cyanosis and a short period of apnea during which his condition appears to be critical, but this is soon followed by a deep inspiration and stertorous breathing. After the seizure the patient either falls asleep or shows a confusional state of variable duration.

The neurological findings correspond with those observed in epileptic seizures. The blood pressure rises 25 or 30 m.m. Hg., and the pulse rate rises from 120 to 140 per minute. I would like to mention some peculiar movements the patient frequently exhibits during this period: rubbing movements in the gluteal and anal regions, coitus-like movements, manipulation with the scrotum, pursing movements with the lips, etc. For the psychoanalytical-minded psychiatrist the door is open for various speculations. Incontinence of urine or ejaculations are not a rule. At no time have we seen a rectal incontinence, even when no enema had been given before the treatment. Tongue bites are prevented by rubber gags or gauze tampons, which are inserted in the patient's mouth at the beginning of the tonic state in which the mouth is opened.

The only complications we had in 450 individual injections among our patients were a dislocation of the right humerus in a young, very muscular 23-yr.-old boy and a dislocation of the jaw in another male patient. A recurrence of these incidents could be prevented by pushing the shoulder down and holding the patient's arms to side and also pressing the lower jaw upward as soon as the tonic phase of the convulsion begins. An open mouth during the clonic phase points toward a dislocation of the temporomandibular joint.

Concerning our results we are able to give only a preliminary report because in some of the patients the treatment has not yet been finished. Naturally these cases have to be excluded from consideration, but it is worthwhile mentioning that 9 of the 21 patients, who have not as yet had sufficient treatment, already show improvement. Up to the present time we have been administering metrazol to 39 patients, 21 male and 18 female patients. Among these are 11 catatonics, 25 hebephrenics, 1 paranoid type, and 2 manic depressive, stuporous form. The ages range from 20 to 48 years. The length of illness has varied from 3 weeks to 9 years. In 13 patients the treatment has been finished with the following results: 12 much improved, 1 unimproved. Eight of the much improved patients have recently been sent home for trial visits and some of these report at regular intervals at the hospital. All these patients are restored to their original condition, do not show any psychotic manifestations, and a few of them have taken up their former occupations. In classifying these cases in relationship to the duration of their illness and regarding cases with a duration of less than one year as acute, those with a duration up to two years as sub-acute, and the ones of more than 2 years' standing as chronic, we have the following figures: 7 patients in the acute, 3 in the sub-acute, 3 in the chronic stage. From the chronic group a 23-yr.-old hebephrenic patient, who has been sick for about 3 years, did not improve in spite of 26 treatments. It should be mentioned that this patient is practically blind and psychotherapeutic measures were extremely difficult to institute because of the above handicap. From the 13 finished cases 9 are cases of hebephrenia and 4 of catatonia. Our figures indicate that cases of short duration show better therapeutic results than those which are of long standing. Because of the short period of time which has elapsed since we introduced the treatment at our hospital, we are, of course, unable to make definite statements about the permanency of the remission. The longest time a patient has been out of the hospital without a relapse is 8 weeks. One 24-yr.-old catatonic patient, who had very extensive treatment and who made a considerable improvement, was sent home for a three-day visit, but was returned with full-

fledged catatonic phenomena. Possibly the extremely unfavorable home environment was the partial cause of his setback.

Although we are not as yet able to report very representative figures concerning the results of the treatment, we are convinced of its effectiveness. It is simple, inexpensive, and relatively without danger. In conclusion I would like to state that although the effect of metrazol treatment is by now well known, the mechanism of this effect is still obscure. Nevertheless, by further intensive clinical and experimental work much light will be thrown not only on this treatment, but inevitably on the structure of schizophrenia, thus contributing to a greater knowledge of the entire problem. The collaboration of the old-school psychiatrist with his healthy scepticism and the enthusiasm of the younger psychiatrist will be a valuable asset toward an impartial understanding and evaluation of this treatment.

BIBLIOGRAPHY

1. von Meduna, L.: New methods of medical treatment of schizophrenia. *Arch. Neurol. and Psychiat.*, 35: 361-363, (Feb.) 1936. Die Konvulsionstherapie der Schizophrenie. *Psychiat.-neurol. Wehnschr.*, 37: 317-319, (July 6) 1935. Versuche über die biologische Beeinflussung des Ablaufes der Schizophrenie; Campher- und Cardiazolkrämpfe. *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 152: 235-262, 1935.
2. Friedman, E.: Irritative therapy of schizophrenia; practical application and theoretical considerations. *New York State J. Med.*, 37: 1813-1821, (Nov.) 1937.
3. Finkelman, I. and Co-workers: The treatment of schizophrenia with metrazol by the production of convulsions. *J. A. M. A.*, 110: 706-709, (March 5) 1938.
4. von Meduna, L.: Significance of the convulsive reaction during insulin and cardiazol therapy of schizophrenia. *J. Nerv. and Ment. Dis.*, 87: 133-139, (Feb.) 1938.
5. Sakel, Manfred: On the significance of the epileptic convulsion as a therapeutic factor in the pharmacological shock therapy of schizophrenia. *J. Nerv. and Ment. Dis.*, 87: 140-155, (Feb.) 1938.
6. Low and Co-workers: Metrazol shock treatment of the "functional" psychoses. *Arch. Neurol. and Psychiat.*, 39: 717-736, (Apr.) 1938.
7. von Angyal, L. and Gyarfás, K.: Ueber die Kardiazolkrampfbehandlung der Schizophrenie. *Arch. f. Psychiat.*, 106: 1, 1936.
8. Finiels, L. A.: Induced epileptiform attacks as a treatment of schizophrenia. *Lancet*, 233: 131, (July 17) 1937.
9. Gillies, Hunter: Convulsive therapy in schizophrenia. *Lancet*, 233: 131-132, (July 17) 1937.
10. Luxenburger, H.: Rückblick auf die wissenschaftlichen Sitzungen der III Jahresversammlung der Gesellschaft Deutscher Neurologen u. Psychiater, München, 20-23, IX, 1937. *Deut. med. Wehnschr.*, 1937, No. 46, pp. 1750-1752 (Nov. 12).

DISCUSSION

DR. SOLOMON: That was a very good conclusion. I will ask Dr. Rothschild if he will open the remarks somewhere midway between the old and the young.

DR. D. ROTHSCHILD (*Foxborough State Hospital*): Dr. Michelson is to be congratulated for his excellent paper and for the work that this paper represents. Our own work at Foxborough has been started too recently (about two months ago), and the cases are too few in number to allow us to contribute any concrete figures to his results, so that this discussion must be confined largely to general impressions, with one or two examples here and there. We have in general conformed to the methods of procedure described by Dr. Michelson, favoring the more conservative method of giving only two or three treatments per week.

Dr. Michelson mentioned a case which might be used to corroborate von Meduna's theory that favorable results of metrazol treatment are due to some mysterious biological antagonism between epilepsy and schizophrenia; but I think we can find other cases which fail to bear out von Meduna's theory. For example, there are at least two schizophrenic patients at Foxborough who later developed what appeared to be epilepsy without showing any beneficial effects. We do not know

what idiopathic epilepsy is, but the fit of idiopathic epilepsy is regarded as the culmination of much more complex and deep-seated disturbances. It is highly improbable that the fit artificially produced by metrazol duplicates this deep-seated process. I think I am in agreement with most students of the subject in rejecting von Meduna's theory. At the same time, I must confess that I am unable to advance any more acceptable theory myself. Before this can be done, much study will be required. I think we should direct our attention to the more immediate effects of the drug or the convulsions on the brain. The convulsion itself is probably produced by cerebral vasoconstriction followed by vasodilatation, that is, cerebral anaemia followed by hyperaemia. Among other parts of the nervous system affected, the brain stem seems to be intimately concerned in the convulsive attacks. Some of our observations which suggest active participation of the brain stem are transient pupillary changes and transient ocular palsies after seizures. Also, the extensor spasm that occurs during the tonic phase of the seizures seems more prominent than in the ordinary epileptic convulsion, and this spasm is very reminiscent of decerebrate rigidity, which is something of a brain stem phenomenon. I mention these features because I don't think they have been stressed enough. Attention has been focussed chiefly on the cortical effects of the drug, yet it is possible that its action on the brain stem, with its vegetative centers, may play an important rôle in the treatment.

Metrazol therapy offers interesting problems in the psychological sphere. For instance, we have noticed, in common with other observers, that fear of dying is almost a regular occurrence in our cases; also, erotic phantasies are frequently stirred up. These features need further study. To my mind it is quite possible that psychological factors play a considerable part in the results of this treatment; just how much remains to be seen.

It should not be forgotten that metrazol therapy produces abnormal changes in the brain, even though these changes may only be transitory. In this connection it might be of interest to mention one of our cases. In this case the psychosis, which was marked by rather complex psychological disturbances, became reactivated as the treatment progressed. The patient became more and more uneasy, fearing that the treatment was affecting his mind, and he finally made a suicidal attempt on the morning before the 12th treatment was to be given. After a few days he seemed to quiet down and returned to his usual state, and he was then given another injection of metrazol, which produced a major seizure. This was his eighth seizure. On the afternoon of that day he went into a rather alarming state in which he remained lying rigidly in bed with some twitching of the facial muscles. He seemed to be in a state of extreme emotional turmoil, and he showed very rapid respirations, a pulse rate of 130 to 160, and a temperature of 101.8. This continued during the day but disappeared within twenty-four hours without leaving any bad physical effects. In another case we noticed a positive Babinski sign persisting over-night but then disappearing. I do not mention these experiences to discourage the use of metrazol. I merely wish to emphasize that the drug should be handled with great respect. I think that metrazol convulsive therapy is drastic treatment, but schizophrenia is such a grave psychosis that radical therapy is fully justified. We are beginning to get a shower of reports in the American literature, most of them highly favorable. From my own experience I personally am not ready to express any definite opinion on the ultimate efficacy of metrazol therapy. I can say this: there is no doubt that metrazol produces changes in schizophrenic psychoses; whether these changes are always beneficial or not and how lasting the benefits may be are questions to be answered in the future. Anything that is able to change a psychosis such as schizophrenia deserves our very serious consideration. I hope therefore that the example set by the Northampton group and other groups will stimulate us all to give this therapy the thorough trial and careful study which I think it merits.

DR. SOLOMON: There is no question that there are two facts that we want to know about in relation to both insulin and metrazol therapy, first, what the clinical effects are, and second, what happens actually to the organism as the result of the treatment. That is true in any radical procedure. There must be a certain amount of danger in these methods, as we know. Just what happens to the brain with metrazol convulsions is a matter of a good deal of concern, at the same time a good

deal of interest in determining how whatever result obtained is obtained. I think that we probably shall be able to hear from some people who are interested in epilepsy and who have a very strong feeling that a convulsion is a dangerous procedure whenever it occurs. I am intrigued by the fact that in both these methods there is a good deal of evidence that the brain receives some damage. There is a certain similarity there with what happens in the so-called Monaz' operation in cutting the sub-cortical connections. There is a growing amount of evidence that damage to certain parts of the central nervous system has a definite effect upon the psychological activities of the individual. That is true, of course, as we see in brain tumors. In the limited experience at the Psychopathic Hospital, we have one case who has shown definite neurological pathology following metrazol which has been fixed and lasting, not fleeting.

I hope that someone in the discussion will take up some of this material of what actually happens in the central nervous system. I wonder if Dr. Davis is here. Would you want to tell us something of the electroencephalographic changes in metrazol?

MRS. HALLOWELL DAVIS (*Harvard Medical School, McLean Hospital*): I think it is rather premature to say anything now, but Dr. Sulzbach and I have been following a long series of metrazol treatments and later on will be able to analyze it. There are some profound changes which we think are very important, but we haven't had a chance to get at the data yet.

DR. SOLOMON: But there are definite encephalographic changes?

MRS. DAVIS: Yes, very definite.

DR. WILLIAM L. HOLT (*Worcester State Hospital*): Following up Dr. Solomon's question, namely, is there damage done to the brain by metrazol, I want to mention the fact that I think it is important to do a lumbar puncture in a patient who is about to receive metrazol injections. I think it is quite as significant to the patient's condition as to do an N.P.N. or blood sugars as done by the author. I have been doing lumbar punctures before metrazol in a number of patients and have done a few on patients who have completed treatment, and have tried in every case to do my second lumbar puncture on the day of a fit near the end of the course of treatment to see what, if any, changes are apparent within a few hours of the treatment. I may say that I have to date only done this on 12 cases, obviously far too small a series to be of much significance. However, the 12 do show an average of 30 red cells more than before the metrazol treatment. The majority of those red cells were fresh. Most occurred in 2 or 3 patients whose taps may have been due to a defect in technique. Another fact that is of more importance, perhaps, is a rise in the total proteins. Again the rise is small and the series of cases small, but there was a rise in the total protein which I take to be a more or less objective measure and perhaps not so apt to vary with the technique of examination of spinal fluid. The greatest number of cells was 200, and the thing I thought significant was that a fair number of patients had some old, partly decomposed red cells present, and that I take to be evidence that there had been some hemorrhages occurring on days previous to the lumbar puncture. May I say that the original lumbar puncture was done at least a month before the second one, so I don't think the old red cells found were due to the first lumbar puncture.

DR. SOLOMON: Any further discussion?

DR. LOUIS H. COHEN (*Worcester State Hospital*): It is only natural, I suppose, that my attitude should be somewhat defensive, since I have been identified rather closely with metrazol treatment at Worcester for a considerable period of time. I have already gathered material on more than 100 patients who have received a total of some 2500 treatments, and who have had a total of almost 2000 seizures.

I do not wish to decry the significance of any pathological changes, especially of a hemorrhagic sort, which may occur in the central nervous system of these patients. It must be pointed out, however, that of all deaths reported to date, none have been brain deaths with the possible exception of that noted by Esser and Kuhn (*Arch. f. Exp. Path.* 171, 1933, 284-288) in a 22-year-old laboratory assistant who swallowed 10 grams of metrazol in a suicidal attempt. They found hyperemia and early thromboses, but the brain itself—both ganglion cells and glia—was not affected. In a single patient of ours who committed suicide 2 months after treatment had stopped, no brain changes were found.

I must take exception to Dr. Holt's statements, since I think the impression gained from his observations is not altogether correct. The average value of 30 R.B.C.'s obtained in the cerebrospinal fluid in his group of 12 patients represents an average which includes 2 bloody taps; if one excludes these two instances, the average R.B.C. count is entirely within normal limits. Similarly, I do not feel that the average rise of 4 mgms. of protein can be considered significant on the basis of the same data.

I think the patient with a persistent neurological defect mentioned by Dr. Solomon deserves more serious consideration. Although I am not at all familiar with the case, I would guess that the patient may have had a hemorrhage because of the raised systolic pressure which is characteristic of the seizure. Dr. Michelson, in his highly instructive and interesting paper, mentioned that during the fit the systolic pressure rises 25 to 30 mm. of mercury. In my experience this is a much lower value than is usually the case; I have found the systolic rise to be from 100 to 200 mm. of mercury. If this is so, and Low et al. (*Arch. Neur. and Psychiat.*, 39; 717-736, April, 1938) have obtained similar effects, initial hypertension must be considered a contra-indication to metrazol treatment.

It would appear from reports now available that metrazol treatment has already shown itself to be no more dangerous than insulin treatment. In fact, it still remains to be shown that it is as dangerous.

In agreement with Dr. Michelson's observations, I would like to point out that as far as the initial convulsant dosage is concerned, with 3 cc. of 10 per cent metrazol one can produce the initial seizure in 7 out of 10 women. In men the threshold is higher, about 5 cc. The problem of the rise in convulsant dosage as treatment progresses is one which has not yet been worked out. I do not believe, from my own experience, that the more advanced the psychosis, the more metrazol is required. Dr. Michelson's method of giving metrazol three times a week combined with psychotherapy is very interesting, but I do not think that one can yet say that this should be the method of choice. One must first know what the advantages of metrazol treatment alone, and of psychotherapy alone, are before one can evaluate the advantages of the combined methods. At Worcester the routine procedure at present is to treat patients daily without any attempt at other forms of formal therapy.

With respect to therapeutic results, I think that this comment may be made. Generally, three groups of patients may be considered. First, those relatively "fresh" patients who reside on quiet wards and make fairly good hospital adjustments but are not well enough to go home. These patients do very well, the catatonics especially, with the paranoid group second, and the hebephrenic group last. Second, the group of mute, negativistic patients. These patients do quite poorly, and relatively little therapeutic effect may be expected. Third, the group of patients on the back wards, the violent, disturbed patients, who are assaultive, destructive, and untidy. These patients are a familiar group in every mental hospital and offer probably the most costly and difficult institutional problems. These patients do quite well. One can expect that after treatment there will be a marked diminution of destructiveness, assaultiveness, and untidiness, changes which may occur in a quite dramatic manner (*Am. J. Psychiat.*, in press).

With respect to the rationale of metrazol treatment, it seems that we are still in the dark. The theory which Meduna presents, namely, that of a biological antagonism between epilepsy and schizophrenia, is not based on adequate evidence. There is not sufficient data on hospitalized schizophrenics and epileptics, let alone of non-hospitalized schizophrenics and epileptics, to make any valid conclusion concerning an antagonism between the two diseases possible.

The fear of treatment as the effective factor has been mentioned by Dr. Rothschild: I think it can be stated (Low et al., *supra*) that the fear of the treatment plays no important rôle. But, the question arises as to whether the fear induced *after* the injection, and which may be forgotten or repressed, is significant in the therapeutic outcome. Work on this problem is in progress at the present time; it may be stated as a preliminary finding that this factor cannot be considered the determinant. The implication remains, therefore, that the *grand mal* seizure is a *conditio sine qua non* of therapeutic efficacy.

DR. SOLOMON: I think that you will all agree that Dr. Bryan has been very successful as an impresario. Now he will show us how good he is as a host.

TREATMENT OF THE TOTAL ORGANISM
IN SCHIZOPHRENIC PATIENTS

By WILLIAM CORWIN, M.D.,
Metropolitan State Hospital,

and

JOHN W. THOMPSON, M.D.,
The Fatigue Laboratory, Harvard University

INTRODUCTION

The traditional concept in psychiatry has been that mental disease is the resultant of a pathologic or psychopathologic locus resident in the central nervous system. Some of the psychoses have been definitely correlated with diseased structures of the brain. In others, particularly schizophrenia, many efforts have been made to discover specific changes in the brain tissues which would account for the mental symptoms. Despite the findings of some neuropathologists, as yet no such correlation has been generally accepted.

It is not unreasonable to suppose that some forms of mental disease might be the end result of a disturbance in function of some anatomical system or systems other than the central nervous system. This is a commonly accepted point of view in other medical specialties. We know, for example, that heart failure can occur as a result of lobar pneumonia, and that a lowered kidney function can produce uremia with consequent mental disturbances.

It is part of our medical training to regard the organism as a composite of separate organs or systems and their functions, and to treat diseases of these organs from this point of view. This similar attitude has existed generally in psychiatry. For some years, however, the dualistic notion of mind-body relationship has been giving way to a monistic conception of the organism where the individual is regarded as a unit of integrated activities existing in interdependent relations with its environment as well as with its component parts. From this point of view it is necessary to treat the organism as a whole unit, and any restitutive efforts must necessarily be directed not towards the one organ which seems to be affected but towards the entire socioindividualistic economy. We have been particularly interested in the application of these concepts to the group of the so-called schizophrenic psychoses.

In recent years increasing attention has been focussed on the factor of deficient oxygenation of the cortical cells in the schizophrenic states. This theory of anoxemia, so-called, is based on the presence in many schizophrenics of a poorly developed and inadequately small heart, associated with a correspondingly smaller vascular tree. The frequency of low blood pressure, cyanosis of the extremities, and perhaps other vasomotor disturbances are well-known clinical findings in these conditions; these we had thought might have been associated with deficient oxygenation. Furthermore, it has long been known to physiologists that a diminution in the oxygen tension of inspired air can produce mental symptoms. Individuals exposed to prolonged conditions of low oxygen have shown reactions similar in some instances to states seen in schizophrenia. Haldane, Kellas, Kennaway's experiences quoted by Barcroft (1) might be cited as an example of the dissociation, disturbed affective reactions, and impaired insight and judgment that can occur. The possible correlation of deficient oxygenation of the central nervous system and psychotic states has interested us and has led to certain experimental investigations. These have been chiefly the estimation of the gaseous content of venous and arterial blood, removed from the jugular vein and femoral artery respectively, simultaneously recording the type of respiration, and in some cases determination of the cardiac output. This procedure has been carried out on a group of patients carrying the hospital diagnosis of schizophrenia, and has been reported in part elsewhere (2). The results obtained compared with figures in non-schizophrenic individuals have shown in general increased carbon dioxide content of arterial blood and high blood respiratory quotients. The respiratory curves have shown small tidal air and a marked regularity in the rhythm of breathing, relatively uninfluenced by external stimuli, such as insertion of needles in blood vessels. Cardiac output in the few patients tested have demonstrated small stroke volume and cardiac index. These observations have been repeated in the same individuals and have shown consistent results, whereas the control group has shown greater variability. All the findings in the schizophrenic group have been present to some extent in the non-schizophrenic group, but none of the latter has shown the constancy or present the combinations of these phenomena to the same degree as the schizophrenic. It has appeared to us that the physiology of the schizophrenic is relatively fixed or set, one not readily adaptable to the constant changes of the internal and external environment. This poorly adaptable state has its psychological concomitant in the personality of the schizophrenics, aptly described as "shut-in", withdrawing instinctively from all

contacts presenting too great a demand, and determinedly 'pursuing a groove-like type of existence.

Although these inquiries have had to do with the circulatory system, and our first impression was that it was the important factor, we have more recently felt that there are other elements equally as important. From the organismal point of view, a disturbance of one organ or system leads inevitably to changes in the entire body, directly affecting the efficiency and state of normalcy of the individual. It cannot be said that the heart is more necessary to the function of the individual as a unit than are the lungs or the kidneys or the nervous system. In attempting to understand disease the tendency, however, is to concentrate on one organ or system and to isolate and treat, if possible, the element that seems abnormal and to be the cause of impaired function. Furthermore, it is our strong feeling that one may be dealing in cases of schizophrenia with systems which individually operate within normal limits but whose integration is improper; in other words, there may be errors of integration and not of systemic mal-function.

There is one other consideration which seems to us may be essential to the proper understanding of schizophrenia, i.e., the time relationship. The method of the "physiological microtome" is not applicable, we believe, to the adequate estimation of the human organism. We feel that a study of the totality of response, i.e. the integrative physiological approach, considered with time as one of the coördinates in any of the observations which are made, is essential to the understanding of the schizophrenic patient.

The treatment of the schizophrenic patient, regarded from this viewpoint, requires a therapy which would counteract the abnormal physiologic state found, and at the same time have an effect upon the total organism. It was the experience of one of us (J.W.T.) that a regime of formal exercises combined with cold stimulating baths was of undeniable benefit to a young schizophrenic hospitalized for about one year. The method to be outlined is an elaboration of this treatment and has been applied to three groups of patients during the past eighteen months.

METHOD

Since our earlier impression was that of disordered circulation or deficient oxygenation it was thought that by exercising the patient in such a way as to induce a greater flow of blood to the head, more efficient oxygenation would ensue. Again by providing for cold shower, particularly on arising, a stimulation to the circulation would result. Our present conception is that the exercises act as a specific stress, taxing the entire organism, and calling forth physiological responses within the organism which necessitate integrative activity. It is felt, therefore, that the physiological stress should not be, in so far as possible, variable or multiple.

In several of the patients another type of stress was used, namely, breathing from air mixtures containing a low percentage of oxygen. These mixtures were prepared by diluting room air with nitrogen, so that mixtures containing as low as 6 per cent of oxygen were obtained. The mixture was inspired through a control valve, and opportunity afforded, if necessary, for the inhalation of CO_2 and O_2 mixtures. The rationale for this procedure was originally suggested by Quastel, (3) and in addition to his view there was the possibility of a gradual acclimatization. As in the case of the exercises, our original idea was altered, and we now feel that by exposing the patient to a condition of relative anoxia, another physiologic stress is imposed requiring the patient to react and to integrate to meet this abnormal state. The increased tidal air, cyanosis, and increased pulse rate are merely indicative of the total response to a particular stress. In essence the end result is similar to the effect of the exercises.

The exercises have been given under the direction of a graduate of a physical education school, assisted by a trained attendant who remained in contact with the group throughout their daily activities. Upon arising each patient was given a cold shower. After breakfast an hour long period of exercises followed, at the end of which another cold shower was given. The exercises and shower were repeated in the afternoon. Both Danish and Swedish exercises were utilized. Until muscular proficiency and physical condition progressed sufficiently, the exercises were relatively simple and performed for the most part in the prone or supine

position. Later other exercises were introduced, many of which, incidentally, are a part of the Yoga system. These latter were found to be difficult except for the more advanced patient. Frequent rest periods during the day were encouraged. Psychotherapy was included, and each patient was seen frequently and rapport established in so far as possible.

RESULTS

The patients treated were all males, all previously diagnosed schizophrenia, and including the several sub-types. Because of the case material available at the time the first group treated consisted of patients regarded as chronic cases whose illness had existed as a rule for several years. Some degree of selection was made, consisting of patients in whom senile changes were not present and who were to some degree coöperative. The other two groups were unselected and consisted of patients hospitalized mostly less than a year.

The results obtained from this method of therapy can be best evaluated by considering them as three groups. The criteria for regarding a patient as improved consisted of increased interest and contact, decrease in apathy and untidy habits, change in mental content and psychotic ideation, development of insight, and improvement in conduct and social adaptation.

GROUP I: This group consisted of thirteen patients of long standing, unimproved illness. The duration of mental symptoms varied from one to eleven years, averaging 6.1 years. Age of patient varied from nineteen to thirty-five years, averaging 27.2 years. Treatment was carried on for periods varying from six to nine months, although one patient was under treatment fourteen months. Of this group, one has been released from the hospital on indefinite visit, and remains out after a period of five months. Of the other twelve, one is considerably improved, three are moderately improved, four are slightly improved, and four remain unimproved, showing no apparent change in mental condition. In three of the cases showing slight improvement, brief periods of overactivity and uncoöperation followed the period of improvement. They have since become quiet and coöperative following cessation of the treatment. The patients have now been off treatment for two months, and improvement persists in those cases who improved under treatment. When resolved into definite figures we find that of the thirteen, two cases or 15.4 per cent considerably improved, seven cases or 53.9 per cent showing slight to moderate improvement, totalling 69.3 per cent of improvement, and four cases or 30.7 per cent are unimproved.

GROUP II: This group consists of four cases whose illness is of relatively short duration, varying from three to twenty months, and averaging eight months. Age varies from eighteen to twenty-six years, averaging 22.2 years. Of this group, one has been sent home on indefinite visit after two and a half months' treatment. The patient was diagnosed hebephrenic type and was considered to be deteriorating rapidly. Another is considerably improved and is being considered for visit. These two received in addition low oxygen inhalation. Of the other two, one has shown definite improvement, while the other has shown no improvement. Treatment of the latter three has, up to the present, extended over a period of three and a half months. Bearing in mind the small number of cases in this group, we have 75 per cent improved and 25 per cent unimproved.

GROUP III: This group consists of nine patients transferred to this hospital for this treatment. Their length of illness varies from five to thirty-nine months, averaging twelve months. Age varies from sixteen to thirty-five years, averaging 23.2 years. Treatment has been carried on for one month, up to present writing. Of this group, six show definite improvement and three remain unaffected and unchanged mentally, yielding percentages of 66.6 per cent improved and 33.3 per cent unimproved.

In all three groups, almost without exception, the physical condition has shown considerable improvement, as would be expected. This improvement is evidenced by increase in weight, improved muscular tone, improved circulation as shown by change from pale, sallow complexion to a healthy, ruddy state, and disappearance of cyanosis and cold moist skin. Where low blood pressure was present, an increase has been noted. In some effected by acne, there was an amelioration of this unpleasant condition.

A few general observations may be made. The paranoid reaction-type has appeared to respond to a lesser degree to the treatment. Good effects have been seen equally among the hebephrenic and catatonic types. There appear to be more favorable effects in the illness of shorter duration. There have been no permanent untoward effects noted, and no phenomena dangerous to the life of the individual have been seen. On the contrary, the physical condition is always benefited rather than injured. When improvement takes place there seems to be a rhythmic cycle of improvement, regression, and increasing improvement until a stationary condition obtains. Considerable individual attention is necessary in withdrawn patients to obtain the coöperation that is essential to the adequate performance of the exercises. Although low oxygen mixtures have been given to only a few patients, it seems to have a synergistic effect. It is interesting and perhaps significant to note that the patient is quite confused mentally for several minutes after returning to room air from an atmosphere containing a low partial pressure of oxygen. Further observations and studies are being made with this procedure. It is our feeling that treatment should be maintained for a period of at least six months before considering the patient unresponsive to this type of management.

CONCLUSION

A method of treatment of the total organism in the schizophrenic patient is presented. This treatment is based upon the concepts of organismal physiology wherein the efficient functioning of the individual is regarded as a total effect of the harmonious and interdependent reactions of all the organs and systems. These concepts do not permit of artificial and confusing separations into mind and body, and other psycho-physical parallelisms. The treatment is without danger to the individual and is, in fact, physically advantageous. In a total of twenty-six patients of varying periods of illness treated up to date, eighteen or 69.2 per cent show improvement varying from slight to marked, while 30.8 per cent remain unimproved; of the eighteen who improved three or 16.6 per cent became more disturbed temporarily, but demonstrated an improved condition at the end of treatment.

BIBLIOGRAPHY

1. Barcroft, Joseph: *The Respiratory Function of the Blood*, Part I, Cambridge University Press, 1925, p. 157.
2. Thompson, John W., Corwin, William, and Aste-Salazar, J. H.: *Nature*, 140: 1062, (Dec. 18) 1937.
3. Quastel, J. H.: Personal communication.

DISCUSSION

DR. GRACE T. CRAGG (*Medfield State Hospital*): Drs. Corwin and Thompson have made some observations which are not only very interesting and constructive, but have been based on a careful investigation by them in some earlier experimental work, of certain physiological effects. The condition which they describe, that is so often found in cases of *Dementia Praecox*, is only too well known to us who have had long State Hospital experience. We are all familiar with the sight of wards full of *Dementia Praecox* cases who are inactive. All their reactions are below normal, and we see that they have mottled and edematous limbs, cold skin, and greasy scalps, etc.

It is interesting to note that many of the psychiatric writers of the early Twentieth Century recognized this condition and described it, and gave considerable speculation and thought to it. They recognized that in many of these cases, above and beyond mental disease there was apparently a deviation in the total organism, and they inferred that there must be some remote cause for these changes. They tended to lay the blame on the endocrine glands, which at that time were becoming the aristocrats of medicine. The subsequent knowledge of endocrines has not made out a clear case against them in *Dementia Praecox*. Whatever the mechanism is at the bottom of these changes, it seems impossible to believe that these factors should be so universally observed in *Dementia Praecox* unless the individuals were following some definite pathological pattern.

I believe that the doctors have conceived a logical theory and have provided some rather impressing figures to support it. I think the authors will agree that the number of cases treated is rather small to give a set of values that are statistically

absolute. However, there is no reason to believe that the cases were selected any more carefully than to provide a representation of our usual Dementia Praecox group, and we may accept their percentages and presume that they are figures that we might expect to find in this therapeutic method.

Now, the numbers given were 69 per cent showing some degree of improvement and 30 per cent unimproved. This seems to reverse the figures found as a result of our routine treatment. The first group seemed particularly impressive, consisting of thirteen cases having a psychosis of long duration, and hitherto unimproved. This group still shows a large percentage of improvement. It seems to me that the term "improvement" should not be taken too lightly. Much of the personal discomfort of our mental patients, the burden of care to the hospital, and their economic inefficiency are due to such traits as uncoöperativeness, noisiness, destructiveness, and untidiness, and if a method of treatment has been found that will overcome these traits, it seems to me it might be well worth adopting.

There is a trend in modern therapy to make use of physical agents, heat, light, electricity, water, and since we must accept the theory that the total organism should be treated in any therapeutic measure used in psychiatry, it seems to me we could adopt this simple method of treating our patients. The practicality of it should appeal to the average staff physician, who perhaps might not have the courage or the time to employ the more sensational therapeutic techniques.

As a result of the figures shown us today in metrazol, insulin, and finally exercise, I think we do well to remind ourselves that behind the wall of inactivity which we call dementia, our patients have certain potentialities of more or less rational action, and if we make use of the tools that have been shown to us we can break through that wall, and turn these potentialities into actualities.

DR. PHILIP SHAPIRO (*Northampton State Hospital*): I'd like to say that in the metrazol session the patient does get a lot of exercise.

DR. D. EWEN CAMERON (*Worcester State Hospital*): I think it would be rather nice to get the statement of the exact exercise procedures which are carried out. It seems very interesting.

DR. SOLOMON: I am waiting to see how long Dr. Hoskins is going to restrain himself.

DR. ROY G. HOSKINS (*Harvard Medical School*): The crux of all the papers heard this morning, and presumably those we shall hear this afternoon, is the matter of *control*. A certain number of schizophrenic patients, of course, are going to get better no matter what you do, or whether you do anything at all. A certain number, apparently, will also die in the back wards. What has to be shown to permit an estimate of the value of any therapeutic regime is how much the average results have been improved. That is a difficult thing to do in any therapeutic research. Even in case of the common cold, which has had extensive study for a long while, we still do not know what measures are best or how good they are. If you contrast the relative simplicity of getting controls in such problems as that of the common cold with the complexities of research on psychiatric problems, you realize how far we are yet from an adequate appraisal of the value of any of these newer methodologies. The same may be said of the older methodologies also. Indeed, we do not even know how good psychiatry is for psychotics.

Another difficulty that we must keep before us all the time is to determine just how much is being accomplished by personal attention to the patient. Whatever else the schizophrenic may have, he has a lot of friendliness in his system. Mere friendliness is likely to have considerable therapeutic value. So much then for difficulties. These things will ultimately have to be determined on a statistical basis, but the necessary data are not yet available.

One might say a word also about the historical aspects. There is nothing new in "shock" treatments. They have been used for centuries. All sorts of elaborate methods have been employed, and excellent therapeutic results have been claimed. On the other hand mere abuse, such as was common in mental hospitals in the past, was apparently without therapeutic value. So much then for elementary difficulties, and for therapeutic research in general and therapeutic research in psychiatry in particular.

The Chairman suggested that I talk about physiological aspects of the psychosis I have been much impressed by the features Doctor Corwin emphasized. The

poorness of the ordinary run-of-the-mine schizophrenic subject as a physiological mechanism seems sufficiently apparent. This shows up in a number of ways, including those Dr. Corwin has mentioned. Study of the blood gases, arterial and venous, brings out anomalous correlations. Abnormal relationships among the metabolic factors rather than the individual metabolic deviations seem to be the more significant. Three or four years ago Jellinek and I read a paper before the Association for Research in Nervous and Mental Disease in which a good deal the same formulation was offered that Doctor Corwin has reached, namely, that the schizophrenic subject, as a total organism, is a victim of "metabolic clumsiness," and that the clumsiness is conditioned by quite a variety of factors. I, personally, lay considerable stress on defective oxygen metabolism; that may be at the bottom of the whole psychosis. I am impressed, as Dr. Corwin is, with the similarity of the schizoid picture to the sort of things that are reported by aviators, etc. under stress of breathing low-oxygen atmospheres. By putting together the elements that are reported by normal individuals under such stress one could synthesize a rather convincing picture of "schizophrenia." As a working conception around which to build research, the one which Dr. Corwin put before you is particularly stimulating.

NARCOSIS TREATMENT IN THE PSYCHOSES

By WALTER E. BARTON, M.D.
Worcester State Hospital

We have long sought a potent means of treatment for the newly admitted, over-active, and excited or agitated patient. In Narcosis Therapy, by means of barbituric acid derivatives, we have such a valuable therapeutic aid. It is the purpose of this paper to encourage its use. There has been considerable reluctance on the part of physicians to accept it, although evidence has accumulated to warrant an extensive trial in the affective reaction types. The latest editions of standard text books in psychiatry such as Strecker and Ebaugh, Henderson and Gillespie, and that edited by Henry A. Christian, call attention to the value of continuous narcosis. Perhaps our hesitation to adopt it is occasioned by the feeling that it has nothing to offer that is better than the conventional hydrotherapy and simple sedative measures now in use, or by the lack of adequate personnel to give the constant special nursing care so essential to the safety of the patient.

For many years sedatives have been used in the management of excitements, but prolonged narcosis was first reported in the cure of acute mania by MacLeod (1) in 1900. Some 12 years before this, Griesinger (2) called attention to improvement in psychotics following the use of narcotic substances. It was not until 1922, following Klaesi's (3) published work of his studies in dementia praecox, that interest was aroused. Increased attention has since been given to this procedure. The introduction of sodium amytal accelerated the consideration of narcotizing agents. It was discovered (by Bleckwenn (21) and Lindemann (4)) that after a period of profound sleep, patients who had been for months in a catatonic stupor or in deep depression began to talk, to act in quasi-normal fashion, and to show a steady improvement if such treatment were repeated.

In this country sodium amytal has been almost exclusively used in the production of narcosis. In England somnifaine (closely related to the American product allurate) is preferred almost entirely. Cloettal and paraldehyde have their adherents, too.

The manic excitements and depressions—particularly the agitated form—afford the best field for therapeutic trial, according to Palmer and Braceland (8), who report 81 per cent improvement and recovery in their first series. About 33 per cent of schizophrenic patients, mostly of the catatonic and hebephrenic type, also made social recovery. Palmer (5) reports most success in anxious depressions, particularly in subjects with pyknic body build. Hennelly's (12) experience attests to improvement chiefly in the affective psychoses.

Palmer and Braceland (8) commenced narcosis therapy in 1930. Twenty-six patients were treated. Six out of eight manic depressive cases, two mixed manic-schizoids, and one of three schizophrenics remained completely recovered at the end of six years, when a follow-up study was made of the original series. They also report on 100 cases in a new series. Manic Depressive types showed 60 per cent recoveries, Depressions 33 per cent, Agitated Depressions 25 per cent, Dementia Praecox cases 21.8 per cent recoveries. Their criteria of recovery seem sound. Others substantiate these findings chiefly in manic excitements and anxiety states (5, 12, 15, 16, 17, 18). Meerloo's (6) series contains 500 cases.

Polatin (19) and Horsely (20) report improvements, but a reversion to former behavior when the drug is withdrawn. Conduct is better, resulting in fewer accidents and injuries and less destruction, without any real change in mental content.

Palmer (5), in an excellent survey of the literature, has selected from the many theories of its action the following:

1. Psychotherapy.

He states that enforced sleep and the artificial invalidism facilitates contact with the patient and makes him more accessible to suggestion. The constant presence of the nurse and doctor aids this. Repeated positive statements that give assurance of recovery are all that are attempted during the period of narcosis itself. One does not delve into deeper problems at this time.

2. Somatic Effect.

Meerloo (6) suggests that the somatic effect may be due to the pharmacological properties of the drug, furthered by the alleged tendencies of barbiturates to exert a specific action on sub-cortical regions.

Müller (7) as quoted by Palmer (8) "Believed the effect was dependent upon central anaesthesia with interruption of the vicious circle of affective

agitation and motor agitation. He concluded that sleep and the interruption of disease functions by means of tissue rest constitute the chief therapeutic effect." Shapiro (9) suggests the action of sodium amytal is in the hypothalamus.

3. Psychodynamic Effects.

Boss (10) is quoted as stating that the ego is a functional psychic organ for whose differentiation and maintenance a certain degree of mental energy is necessary. Sleep rests forces which maintain the ego in consciousness. In the normal this occurs satisfactorily, but the mechanism fails in dementia praecox. The marked change in behavior and the less pronounced alteration in the emotional attitude occur on the basis of release of inhibitions. Inhibitions arising from social conditioning are represented in the cortex (Lindemann (4)).

MacDonald (11) holds that prolonged sleep interferes with habitual modes of thought and action. The enforced rest fosters selection of new habits of thought and action, similar to "sleeping over one's problems." The excited patient often voices the feeling—"If I could only sleep, all would be well."

Technique. (Modified from Palmer and Braceland (8)).

The procedure has been found to be without danger if a few safeguards are taken. In general one should select patients adequately hydrated and nourished. Those who have marked arteriosclerosis and myocardial damage must be rejected. It is also best to eliminate those cases who have a focus of infection that might become activated during the treatment. Müller (13) reports 5 per cent mortality. Few other observers report fatalities. With care in selection of risks, and constant observation during sleep, by trained personnel, hazards are almost nil.

A quiet darkened room is essential to uninterrupted sleep. No visitors or letters are permitted. A special nurse on duty at all times may be expected to handle six patients.

The reaction to Sodium Amytal is first tested by the oral administration of 6 grains at night. The next day 6 grains are given three times. Each day, or if necessary each dose, is increased by 3 grains until the drug is sufficient to produce sleep, with quiet restful slumber. To accomplish this, the nurse must be allowed some latitude in the time the next dose is to be given instead of adhering to a rigid schedule of dosage every three or four hours. As soon as the patient rouses and becomes restless the amount specified is given and the doctor notified; he then adjusts the dosage schedule. Within four days, dosage is established that enables a fairly constant quantity of the drug to be administered at three-hour intervals. From 24-93 grains of sodium amytal daily was necessary to maintain the usual level desired. In a case of Palmer's (8), 220 grains were given in a day. The oral method is the one of choice, but if refused, one or two doses of $3\frac{3}{4}$ grains intravenously will usually make it possible to continue by mouth.

Twice daily the patient is given general nursing care with bed bath and attention to bowels and bladder. He usually awakens easily—is drowsy and unsteady but may sit up for toileting. He may eat his 2500 calorie meal at a table. Fluids to 2500 cc. are required, with intake and output carefully recorded.

Insulin and glucose, stressed as important by users of somnifaine, are not needed with amytal. An adequate intake of fluids apparently prevents the appearance of acetonuria.

During the period of sleep the nurse must frequently change the position of the patient and see that he has sufficient covering and protection from drafts.

After 10-14 days medication is gradually withdrawn by halving the dosage of the previous day. This requires three to four days. Continuous tubs and general ultraviolet irradiation are useful during this phase of the treatment.

It is very important to place the patient at work at the earliest possible time after the above procedures have terminated. The first day the dosage is halved, he is placed in the continuous bath at night and exposed to generalized ultraviolet irradiation in the morning. The remainder of the day he spends in the occupational therapy shop. A task that he can work at alone, apart from immediate stimulation by other patients, is selected. Such introduction of industry utilizes that period of clarity that usually follows shortly after the narcosis ends, and serves to establish the feeling of normality. The patient should be given the benefit of

an early trial at home, as relapses occur frequently if such trial is delayed. All emphasis is directed toward showing the patient that something has transpired to make him different and that now he is well enough for a visit at home.

The most frequent complications reported by others are fever, vomiting, retention of urine, convulsions, aspiration, pneumonia, and low blood pressure. One of our patients had a convulsion three days after the completion of the treatment. Kearney and Courtney (14) had a similar experience.

We keep a bedside emergency tray in the room with ampules of coramine, picrotoxin, ephedrine sulphate, adrenalin, and caffeine, as well as sterile syringe and intravenous equipment. A mouth gag and tongue forceps and catheter for aspiration may also be of use.

Illustrative of our brief experience, we cite the following examples. A 41-year-old male, with a positive history of mental illness in a grandmother and cousin, was admitted to our hospital on November 27, 1937. He was a painting contractor, happily married some nine years to a school teacher. He preferred solitary activities, was rather shy, and his social life centered entirely about his wife. In September, 1937, two months before admission here, he had his third attack of pneumonia and was very ill. During his sickness his father became weaker and died in November of heart disease. The patient developed a fear of heart disease, cancer, and leprosy. He believed the doctors felt his case to be hopeless. He paced the floor restlessly, and expressed the belief that he was to die in the electric chair for kissing a girl. For two weeks after entrance he was confused and depressed, heard the radio talking to him, and felt that the patients were G-men and that he was drowned in the tubs. He made an attempt at escape, broke glass, and became so agitated that his eight hours of continuous baths were changed to wet sheet packs for two days. The acute episode subsided but he continued depressed, anxious, and hallucinated and deluded. After two and one-half months without change, narcosis therapy was instituted and continued fourteen days. The maximum daily dose was 75 grains of sodium amylal. The third day after withdrawal he suffered two generalized clonic convulsions. At this time he had a rather severe glossitis. The improvement that was noted at the end of his treatment became increasingly evident and in twelve days he went home overnight. His wife enthusiastically reported that he not only seemed normal, but he was able humorously to discuss the substance of his former anxieties without a trace of discomfort. After a four-day trial he was released on indefinite visit, three weeks after the conclusion of the narcosis treatment. He is at present employed at his old job. His effective response is quick and normal and all traces of abnormality are gone.

The second case is that of a 52-year-old manic depressive, manic excitement, admitted November 23, 1937. His ancestry is free from taint of mental illness. Born in Russia, he came to this country in the direst poverty at 17. His rise from "rags to riches" in the junk business was dramatic and at the time of his first attack in 1926 he was said to be worth \$300,000. He was 41 when first taken ill, was typically overactive and excited, turned against and threatened his wife. This episode lasted two months. He was well only eight months before he suffered a profound depression. Since that time he has had four attacks, the last in 1932. He returned home in nine months after his excitement abated, but wasted his money, drank, was promiscuous, and would have nothing to do with his wife. During this interval he never regained his prepsychotic status.

On admission here he was grandiose, elated, overactive, wildly excited, pushing and getting pushed by other patients. His nursing care was most difficult due to his insistent demands.

After one month, during which he failed to respond to hydrotherapy, he was placed on sodium amylal narcosis treatment that was continued for sixteen days. The maximum daily dose was 93 grains. The first twelve days during his waking moments he was restless, irritable, and demanding. Then he became quiet and coöperative and four days later treatment was terminated. For three days he was quite normal. He talked about his business and apologized for the behavior during his excitement. He became increasingly insecure and then more and more depressed, and has remained now in this retarded stupor for three months.

The third case had had six previous episodes of excitement and depression, the first at 17 years of age. Duration of hospital stay varied from six months to four

years. The last attack had been the shortest and occurred sixteen years previously. He was 61 years old on entrance August 13, 1937. For 25 years he worked as a maker of horseradish. There was no living relative to whom he could turn for aid or consolation when he lost his job. He was excited, overactive, mischievous, and constantly talking with great push of speech. Narcosis treatment was given six months after admission for twelve days. With a maximum daily dose of 49 grains he was no better. Two months later he was sufficiently improved to permit transfer to a quieter ward and he went to work in the hospital laundry. He is still mildly excited and talkative.

Case number four is that of a 64-year-old man with early arteriosclerosis and a history of excessive alcoholism. Four years ago he spent five months in this hospital. At that time he entertained a belief that his wife and daughter were immoral. In November, 1937, he developed a wild excitement, and was noisy and overactive. He believed his daughters' husbands were sticking knives into his daughters' backs and thought his wife unfaithful.

One month after admission he was given fourteen days of narcosis treatment. He was better for a week and then relapsed. Two months later, in spite of hydrotherapy, he was much more excited than on admission. He was then given a second course of sodium amylal narcosis lasting fourteen days, with a maximum daily dosage of 56 grains. He was markedly improved as the treatment ended and a week later was permitted to go home. He appeared slightly retarded in activity a month later, but protested he felt fine. He has remained at home now four months.

The last case was that of an 18-year-old boy exhibiting a hypomanic reaction. He was restless, unmanageable, attempting escape, swaggering, self-confident, and bursting with a new idea each hour, which he sought to impress upon any who would listen. The background held a suspicion of encephalitis, but the predominant pattern was that of a psychopathic personality. Sixteen days of narcosis therapy were given after three months of hospitalization with a maximum daily dose of 84 grains.

At the end of treatment he was a little more coöperative, less quarrelsome, and no longer bubbling over with enthusiasm and ideas. His parents removed him from the hospital at once, as they were convinced he had recovered. We did not share their opinion, but he has remained well adjusted at home for four months.

Although Case 1 may well be said to have had a hopeful prognosis, the improvement did not begin until narcosis treatment was completed. The second case showed a change in his mental reaction twelve days after the commencement of therapy. The period of lucidity and complete change from excitement to one of depression seems related to the therapy. The third case appears not to have been influenced. The late improvement cannot be assigned to the amylal. Case 4 improved temporarily following narcosis, relapsed, and then markedly improved during a second course. The changes in mental reaction seem attributable to the treatment. Case 5 is unconvincing but appeared to improve slightly and has adjusted at home satisfactorily.

The many workers who have accumulated an experience with narcosis treatment have seen fit to continue its use. The brief trial here seems to offer encouragement in that direction.

From these reports it can be said that narcosis is of value in the treatment of mental disorders, particularly the manic phase of manic depressive psychosis and agitated depressions. The period of hospitalization is significantly shortened and a complete remission may be expected in about one-third of the cases.

BIBLIOGRAPHY

1. MacLeod, N.: Bromide sleep. A new departure in the treatment of acute mania. *Brit. Med. J.* 1: 134, 1900.
2. Griesinger, W.: *Mental Pathology and Therapeutics*. Translated by Robertson and Rutherford. William Wood and Company. 1882.
3. Klaesi, J.: Ueber die therapeutische Anwendung der "Dauernarkose" mittels Somnifens bei Schizophrenen. *Ztschr. f. d. ges. Neurol. u. Psychiat.* 74: 557-592, 1922.
4. Lindemann, E.: Psychological changes in normal and abnormal individuals under influence of sodium amylal. *Am. J. Psychiat.* 11: 1083-1091, 1932.

5. Palmer, H. A.: Value of continuous narcosis in treatment of mental disorder. *J. Ment. Sc.* 83: 636-678, (Nov.) 1937.
6. Meerloo, A. M.: On action of barbituric acid compounds; contribution to prolonged narcosis treatment of mental symptoms. *J. Ment. Sc.* 79: 336-367, (April) 1933.
7. Müller, M.: Die Dauernarkose mit flüssigem Dial bei Psychosen, speziell bei manisch-depressivem Irresein. *Ztschr. f. d. ges. Neurol. u. Psychiat.* 107: 522-543, 1927.
8. Palmer, H. D. and Braceland, F. J.: Six years experience with narcosis therapy in psychiatry. *Am. J. Psychiat.* 94: 37-57, (July) 1937.
9. Shapiro, L. B.: Sodium amytal: effects on oxygen consumption rate in psychoses. *J. Nerv. and Ment. Dis.* 85: 305-309, (Mar.) 1937.
10. Boss, M.: Die psychische Dynamik der Schlafkur bei Schizophrenen. *Schweiz. Arch. f. Neurol. u. Psychiat.* 36: 209-220, 1935.
11. MacDonald, J. H.: Somnifaine narcosis; psychological aspects. *J. Ment. Sc.* 82: 429-431, (July) 1936.
12. Hennelly, T. J.: Prolonged narcosis in manic-depressive psychosis. *J. Ment. Sc.* 82: 608-614, (Sept.) 1936.
13. Müller, M.: Die Dauernarkose mit Somnifen in der Psychiatrie. Ein Ueberblick. *Ztschr. f. d. ges. Neurol. u. Psychiat.* 96: 653-682, 1925.
14. Kearney, J. and Courtney, P. J.: Somnifaine narcosis: Results of 40 treatments in 38 cases. *J. Ment. Sc.* 84: 177-182, (Jan.) 1938.
15. Parfitt, D. N.: Treatment of mania. *J. Ment. Sc.* 82: 615-617, (Sept.) 1936.
16. MacNiven, A.: Somnifaine Narcosis; clinical aspects. *J. Ment. Sc.* 82: 423-429, (July) 1936.
17. Verstraeten, P.: La thérapeutique convulsivante de la psychose maniaco-dépressive. *Ann. méd.-psychol.* (pt. 2) 95: 654-659, (Nov.) 1936.
18. Favre, Andre: Schizophrenies et narcoses prolongées. *Encéphale.* 31: 196-211, (Mar.) 1936.
19. Polatin, P.: Prolonged sedation with sodium barbital of male disturbed continued treatment patients. *Psychiatric Quart.* 11: 213-221, (April) 1937.
20. Horsely, J. S.: Therapeutic narcosis with soneryl. *J. Ment. Sc.* 83: 25-39, (Jan.) 1937.
21. Bleckwenn, W. J.: Narcosis as therapy in neuropsychiatric conditions. *J. A. M. A.* 95: 1168-1171, (Oct. 18) 1930. Production of sleep and rest in psychotic cases; preliminary report. *Arch. Neurol. and Psychiat.* 24: 365-372. (Aug.) 1930.

DISCUSSION

DR. WILLIAM C. INMAN (*Danvers State Hospital*): A paper of this sort doesn't seem to offer much for discussion because of its completeness. However, one school has taken a psychic attitude towards this in that they are using smaller doses of amytal and producing what they call the twilight sleep stage, on the basis that during this stage the resistance of the patient is broken down and good contact can be obtained, and on the basis of that intensive psychotherapy can be instituted. The other school seems to be more on an organic basis, and their theory is to produce a rather deep narcosis and to get the sleep and physiological rest. However, in this too is used some positive direct psychotherapy. The end results seem to be about the same.

It seems that if this treatment is going to be used in State Institutions, several things must be emphasized. First, because of the deep narcosis, permission should be obtained from the nearest relative, and this is because of the dangers that may be encountered in the treatment. Most of the writers report no fatalities, but there have been a few. You must watch for a marked lowering of the blood pressure, marked elevation of temperature, and you must be careful that the treatment is not terminated too rapidly or convulsions will ensue. One writer reports a convulsion occurring nine days after termination of treatment. Another thing, this treatment requires rather carefully trained personnel—nurses who are well adapted to quite forceful, kindly care of the patients, and the physician must devote the greater part of his time to the care of the patients. Patients must be rather carefully selected, focal infections and other organic diseases eliminated.

The treatment must be started carefully so that any idiosyncrasies may be discovered.

In conclusion, it seems that this is a treatment worthy of trial in the acute manics who are great disturbed, and it is a treatment worthy of trial in the termination of tube-feeding.

DR. SOLOMON: What Dr. Hoskins said about controls is even more difficult in the Manic-Depressive group in which one expects slow recovery, and one always is critical, I think. I am offering the criticism that the doctor says one of his patients was a bad risk for prompt recovery, although it would seem that one could readily counter that he made five previous recoveries in relatively short time, so why not this one.

DR. LEON J. ROBINSON (*Monson State Hospital*): I'd like to say a word about the presence of convulsions following withdrawal of amytal. The French literature contains a report on abstention epilepsy occurring in certain individuals who never have seizures, but who are on large doses of sedatives, and following the sudden withdrawal of the latter, these people occasionally have convulsions. It doesn't add anything to the therapy involved, but there is a small group of patients who will occasionally have convulsions following sedation therapy.

DR. WILLIAM A. BRYAN (*Worcester State Hospital*): These papers immediately raise the question of the need of better trained and more ward personnel. To carry on a campaign of active therapy requires the services of specially trained graduate nurses in sufficient number to adequately carry out the specific procedures. Such work cannot be done by attendants. With due respect to the faithful and splendid work our attendants have done, I submit that if we are to approach the problem of mental disease from the standpoint of therapy, the present number of graduate nurses and medical staff must be increased.

I would also call your attention to the fact that treatment procedures can be carried out in old buildings as well as new. It does not need new, finely equipped buildings. If we could suspend our building for a time, and put into personnel the money that we would ordinarily put into buildings, I am sure that twenty-five years from now the State of Massachusetts would be very much better off than it would be if the emphasis were upon the treatment of mental disease by bricks and mortar.

BENZEDRINE SULPHATE—AN ANTIDOTE FOR THE UNTOWARD
HYPNOTIC AND ATAXIC EFFECTS OF PHENOBARBITAL
IN THE TREATMENT OF EPILEPSY

BY BENJAMIN COHEN, M.D.
Grafton State Hospital

and

ABRAHAM MYERSON, M.D.
Boston State Hospital



THE NATURE AND ACCEPTED USES OF BENZEDRINE

Benzedrine (a phenyl-B-amino-propane) (24) is a sympathomimetic compound closely related in chemical structure to ephedrine (a-phenyl-B-methyl-amino-propanol). It was first described in 1910 by Barger and Dale (23) but did not enlist the attention of investigators until 1930. Since then it has received close scrutiny from both experimental and clinical viewpoints.

In 1935 Prinzmetal and Bloomberg (1) reported that this drug was approximately three times as effective as ephedrine in the treatment of narcolepsy and their findings were confirmed shortly thereafter by Ulrich, Trapp and Vidgoff (2).

The pressor action of benzedrine has received much comment. Piness, Miller and Alles (3) observed that both by subcutaneous and oral administration blood pressure was raised. Anderson and Scott (4), however, in six cases noted both increases and decreases. According to Alles (10) in 1933 the pressor effect of benzedrine was less than that of epinephrine. Four years later Detrick, Millikan, Modern, and Thienes (11) found, through animal studies, that the blood pressure-raising power of benzedrine was only 1/500 to 1/100 that of epinephrine.

Clinical studies have brought variable findings. Some patients, during the course of benzedrine medication, have variously shown rises of blood pressure (3, 4, 5, 6, 7, 8, 9, 11, 13), fall of pressure (4, 12, 13,) and stationary levels (12, 13). Individual factors seem to play a large part and pressor effects are not always predictable.

Ulrich (12), employing benzedrine sulphate orally, concluded that blood pressure rise was dependent upon the dose used and did not occur unless more than 20 milligrams was taken at a time.

Myerson and associates (5) noted that amytal, given either before or after blood pressure rise was prone to occur, counter acted such effect.

Oral use of the drug has other effects in addition to those described: Weight may show moderate decrease. Red cells and leucocytes in the circulating blood frequently increase (21). Some patients may note flushing or pallor, sweating, and consciousness of heart action (13). Temperature, respiration, and basal metabolism (20, 21) show no consistent change, and blood sugar (7) and non-protein nitrogen levels (8, 20) are unaffected.

These have been the most striking therapeutic uses and effects of benzedrine sulphate by oral administration:

1. Treatment of narcolepsy. The results have been spectacular (12, 14, 15).
2. Use of the drug alone or preferably in association with scopolamine or stramonium in the treatment of drowsiness, lack of energy, and oculo-gyric crises in post-encephalitic Parkinson's disease.
3. Diminution and abolition of gastro-intestinal spasm (17).
4. The amelioration of mood, alleviation of fatigue (19), and the production of an increased feeling of energy in normal (19), psychoneurotic and mildly depressed persons (9, 18). Davidoff and Reifenstein (13) found the drug of more value in the organic (particularly the alcoholic) depressions than in those of a psychogenic nature.
5. Robinson (22) has described the effective use of the drug in the treatment of syncope due to a hyperactive carotid sinus reflex.
6. Lesses and Myerson (14) have employed benzedrine to correct obesity. It has proven particularly valuable in those cases where mood disorder and over-eating of a compensatory compulsive nature were responsible factors.

TOXICOLOGY OF BENZEDRINE SULPHATE

The toxicity of benzedrine is low (19). The minimum lethal dose for the rat is 25 milligrams per kilogram of weight and for the guinea pig 35 milligrams per kilogram. This is of particularly great interest since the common therapeutic doses in humans are 10 to 20 milligrams.

It is generally agreed that the drug should not be administered to persons suffering from coronary disease or hypertension (9, 19) and to those who are subject to insomnia, anorexia, exhaustion, and manic outbursts.

Persons taking the drug may observe fatigue, restlessness, insomnia, and vasomotor complaints.

Since benzedrine and the barbiturates are at least in part pharmacologically antagonistic, (21) the untoward effects of benzedrine may be terminated by appropriate doses of barbiturates (20). Insomnia may be usually prevented by restricting medication to morning and noon.

The usual therapeutic doses range from 10 to 30 milligrams daily. Prinzmetal and Bloomberg (1) have used the drug in certain cases for over a year without untoward effects. Other authorities have noted similar findings.

THE EMPLOYMENT OF BENZEDRINE FOR THE RELIEF OF ATAXIA AND DROWSINESS DEVELOPING IN THE COURSE OF PHENOBARBITAL MEDICATION

For over a year, with the assistance of Dr. Nathaniel Showstack (of the Grafton State Hospital), we have been carrying on an organized therapeutic study in epilepsy involving about 150 unselected patients at the Grafton State Hospital. By handling these patients on a project basis, and by adjusting dosages of phenobarbital regularly in accordance with individual seizure rhythm, we succeeded during an average period of eight months in reducing seizure incidence about two-thirds, and in maintaining the improved level. The patients included in this study were saved about 3800 seizures during the last eight months. Estimates of expentancy, wherever possible, were based upon the seizure totals of the two previous years. The following chart offers details of results obtained:

Results of Use of Adequate Phenobarbital in the Treatment of Epilepsy

A. MALE PATIENTS

No. of Patients in Group	Duration of Treatment	No. of Seizures Expected	No. of Seizures Resulting
9	46	1,242	266
6	36	244	53
19	42	1,034	306
33	25	487	170
26	31	736	359
—	—	—	—
Totals	93 Patients Av. 36 wks.	3,743	1,154

B. FEMALE PATIENTS

No. of Patients in Group	Duration of Treatment	No. of Seizures Expected	No. of Seizures Resulting
39	34	1,747	629
9	31	149	35
—	—	—	—
Totals	48 Patients Av. 32 wks.	1,896	664

C. TOTAL FINDINGS

No. Patients in Combined Groups	Duration of Treatment	No. of Seizures Expected	No. of Seizures Resulting
141	Av. 35 wks.	5,639	1,818

Nineteen of our patients developed drowsiness and ataxia due to phenobarbital, many of them becoming so unsteady on their feet that it was necessary to put them to bed.

We found no constant correlation between size of phenobarbital dose and the appearance of toxic findings, as is evident from the following table:

Daily Amount of Phenobarbital	Number of Patients Receiving Such a Dose	Number of Patients Showing Drowsiness and Ataxia
1½ grains	16	2
2 "	26	4
3 "	20	3
3½ "	11	2
4 "	11	2
4½ "	12	2
5 "	8	2
5½-7 "	10	2

In an attempt to find possible predisposing causes, urinalyses, renal function tests, and fasting blood non-protein nitrogen, creatinine, and blood sugar determinations were carried out. Essentially normal results were obtained.

Endeavoring to relieve toxic findings, we gave the patients so affected 5 to 20 milligrams of benzedrine sulphate daily by mouth. Striking clinical improvement was rapidly shown by these patients and maintained in the presence of unchanged dosage of phenobarbital. Six of our patients have received such combination medication for 22 to 26 weeks, and the remainder for varying lesser periods.

The effect of supplementary benzedrine upon seizure incidence is indicated in the following table. Phenobarbital (luminal) dosages were held constant.

Patient	LUMINAL PERIOD		LUMINAL AND BENZEDRINE PERIOD	
	No. of Weeks	Seizures per Week	No. of Weeks	Seizures per Week
C. La. . . .	16	.12	22	.18
J. B. . . .	20	.75	22	.36
W. L. . . .	20	.25	22	.27
F. M. . . .	25	.88	17	.41
A. P. . . .	20	.15	17	.00
N. S. . . .	24	.67	7	.86
E. B. . . .	7	10.85	24	.62
M. D. . . .	16	.63	7	.43
C. Le. . . .	17	.06	14	.07
L. M. . . .	17	.18	14	.28
C. Co. . . .	9	.11	22	.00
E. H. . . .	12	.75	18	.55
C. Ca. . . .	17	.41	13	.69
A. F. . . .	7	1.29	15	.13
M. F. . . .	14	1.77	15	3.00
S. B. . . .	5	.00	26	.19
M. G. . . .	20	.45	11	.18
D. L. . . .	16	5.75	12	7.42
	Total (average)		Total (average)	
	Seizures per Week	25.1	Seizures per Week	15.6

The above table indicates that nine of the eighteen patients in this series had fewer seizures during the luminal period, and nine had better results during the period of added benzedrine sulphate. It is evident that the remarkable advantage in favor of benzedrine was largely due to the improvement showed by one patient. When figures relative to the latter are disregarded, we find essentially no difference in the residual group total for seizures during the two periods.

A striking improvement was shown by patient E. B., a girl who is seventeen years old. Her history indicates injury by high forceps at birth. Seizures since the age of three days. Hemiplegia at the age of two. She now has pyper-extension at the right wrist with flexion of the fingers and a Babinski reflex on the right. Her usual seizure rate was 15.9 seizures per week, many of which were Jacksonian in character. Increased dosage of phenobarbital reduced seizure frequency to 10.9 over a period of seven weeks. She showed drowsiness and ataxia at a dose of 5 grains of phenobarbital daily. The dosage of the latter drug was left unchanged and benzedrine sulphate, 10 milligrams daily, was given for eight weeks. During this period she averaged 1.7 seizures per week. Then the dose of benzedrine was increased arbitrarily to 20 milligrams daily. In the next sixteen weeks she had a total of only one seizure.

Two patients—M. F. and D. L.—showed significant increases of seizures during the benzedrine period. The former has congenital C. N. S. syphilis and the latter (a boy of thirteen) has a diagnosis of idiopathic epilepsy since detailed studies have yielded no explanation for the seizures.

One patient died during the period of benzedrine medication although he appeared to be showing clinical improvement. This patient, age 51, had a diagnosis of idiopathic epilepsy, duration forty-five years. His preliminary blood pressure and urinary findings were negative. His record indicates that from 1933 to 1936 he averaged 1.5 seizures per week; however, adjustment of phenobarbital dosage reduced attacks to an average of .6 per week over a period of ten weeks. Drowsiness and ataxia appeared at a dose of 4 grains of phenobarbital daily, and were entirely relieved by the use of benzedrine sulphate. The patient had benzedrine sulphate for only seventeen days and during this time he had no seizures and appeared to be doing well. Cause of death, as established at autopsy, was due to thrombosis of the left internal carotid artery, cerebral softening, and terminal bronchopneumonia. At no time during the last illness was blood pressure elevated.

In the attempt to gather further information concerning the drug, thirteen unselected cases receiving benzedrine were checked some four to five times at regular intervals over twelve to fourteen weeks for basal metabolism, blood pressure, and pulse rate. The results were inconstant and the variations were entirely within limits of usual expectation.

The weight changes during the period of benzedrine medication were observed in seventeen cases and are indicated in the following table:

<i>Patient</i>	<i>DURATION OF STUDY</i>		<i>Wt. at Onset</i>	<i>Wt. at End of Period</i>	<i>Wt. Change</i>
	<i>Months</i>	<i>Days</i>			
C. La.	4	24	161	165	+4
J. B.	5	24	172	167½	-4½
W. L.	5	29	181	173	-8
F. M.	4	19	143	137	-6
A. P.	4	19	115	107	-8
M. D.	2	6	178	171	-7
E. B.	4	4	102	106	+4
N. S.	2	3	123	108	-15
C. Le.	3	19	132	129	-3
L. M.	3	19	155	151½	-3½
C. Co.	5	21	133	124	-9
E. H.	4	24	115	109	-6
C. Ca.	3	19	157	141	-16
A. F.	3	20	145	126	-19
M. F.	4	2	100	87	-13
M. G.	2	11	147	147	None
D. L.	3	22	112	113	+1
Average Findings . . .	4	1			-6.4

The foregoing chart reveals that thirteen patients lost weight (a total of 118 lbs.); three gained weight (a total of 9 lbs.) and one showed no change. Over an average period of about four months, an average weight loss of 6.4 lbs. per patient occurred.

SUMMARY

1. In the course of a therapeutic study of epilepsy conducted at the Grafton State Hospital, nineteen patients receiving varying doses of phenobarbital developed drowsiness and ataxia.
2. Urinalyses, renal function tests, blood non-protein nitrogen, creatinine, and sugar determinations failed to indicate factors favoring the appearance of toxic findings. Similarly no constant relationship to size of phenobarbital dose could be established.
3. Benzedrine sulphate, given in doses of 5 to 20 milligrams daily, showed the following results:
 - a. Drowsiness and ataxia disappeared rapidly despite use of an unchanged dosage of phenobarbital.
 - b. Benzedrine sulphate, in most cases, had indifferent effect upon seizure incidence. Moderately adverse effect appeared present in a case of symptomatic epilepsy (hereditary C. N. S. syphilis) and in a case of idiopathic epilepsy. A strikingly good effect was noted in a case of symptomatic epilepsy due to cerebral birth injury. (During a control phenobarbital period of seven weeks, this patient averaged 10.9 seizures per week; in the next twenty-four weeks, during which time she received 10 to 20 milligrams of benzedrine sulphate, she averaged .62 seizures per week.) This patient gained 4 lbs.
 - c. One patient died during the period of benzedrine administration from thrombosis of the left internal carotid artery. Since toxic findings attributable to phenobarbital and benzedrine were not recognized and blood pressure findings were consistently normal, there does not seem to be any reason to assume that either drug produced fatality.
 - d. At regular intervals over a period of twelve to fourteen weeks, thirteen patients were checked four to five times to determine blood pressure, pulse, and basal metabolic findings. Variations were scant, indifferent in direction, and within the limits of normal fluctuation.

- e. Weight changes were studied in seventeen cases, thirteen of whom lost weight. The average period of benzedrine medication was four months and the average loss of weight per patient was 6.4 lbs. Loss of weight appeared to be directly due to the use of benzedrine since phenobarbital does not have such effects.

CONCLUSIONS

1. Benzedrine sulphate, continued orally in a total dosage of 5 to 20 milligrams daily, efficiently overcomes the drowsiness and ataxia which occasionally develop in epileptics receiving phenobarbital.
2. Except for loss of weight, the drug (used in the fashion described) appears to have no untoward effects upon seizure incidence or general health.
3. One patient, whose epilepsy was due to cerebral birth injury and who received scant benefit from phenobarbital, became almost seizure-free on a supplementary dosage of 20 milligrams of benzedrine daily; this recommends trial of the drug in similar cases.
4. Although we maintained regular dosage of benzedrine, the occasional use of the drug for the relief of toxic symptoms when they appear seems to be the preferable method of medication in those cases where loss of weight is inadvisable.

BIBLIOGRAPHY

1. Prinzmetal, Myron and Bloomberg, Wilfred: The use of benzedrine for the treatment of narcolepsy. *J. A. M. A.* 105: 2051-2054, (Dec. 21) 1935.
2. Ulrich, H., Trapp, C. E., and Vidgoff, B.: The treatment of narcolepsy with benzedrine sulphate. *Ann. Int. Med.* 9: 1213-1221, (Mar.) 1936.
3. Piness, George; Miller, Hyman; and Alles, G. A.: Clinical observations on phenylaminoethanol sulphate. *J. A. M. A.* 94: 790-791, (Mar. 15) 1930.
4. Anderson, E. W. and Scott, W. C. M.: The cardiovascular effects of benzedrine. *Lancet.* 2: 1461-1462, (Dec.) 1936.
5. Myerson, Abraham; Loman, Julius; and Dameshek, William: Physiologic effects of acetyl-beta-methylcholine (mecholy) and its relationship to other drugs affecting the autonomic nervous system. *Am. J. M. Sc.* 193: 198-214, (Feb.) 1937.
6. O'Connor, D. M.: Benzedrine. *Brit. Med. J.* 1: 43, (Jan. 2) 1937.
7. Peoples, S. A. and Guttman, Erich: Hypertension produced with benzedrine; its psychological accompaniments. *Lancet.* 1: 1107-1109, (May 16) 1936.
8. Guttman, Erich: Some psychiatric observations in arterial hypertension. *Proc. Roy. Soc. Med.* 29: 1387-1391, (Sept.) 1936.
9. Wilbur, Dwight L.; MacLean, Alexander R.; and Allen, Edgar V.: Clinical observations on the effect of benzedrine sulphate; study of patients with states of chronic exhaustion, depression, and psychoneurosis. *J. A. M. A.* 109: 549-554, (Aug. 21) 1937.
10. Alles, G. A.: The comparative physiological actions of d1-B-phenylisopropylamines; pressor effect and toxicity. *J. Pharmacol. and Exper. Therap.* 47: 339-354, (Mar.) 1933.
11. Detrick, L. E.; Millikan, R.; Modern, F. S.; and Thienes, C. H.: On the pharmacology of phenylisopropylamine (benzedrine). *J. Pharmacol. and Exper. Therap.* 60: 56-68, (May) 1937.
12. Ulrich, Helmuth: Narcolepsy and its treatment with benzedrine sulphate. *New England J. Med.* 217: 696-701, (Oct.) 1937.
13. Davidoff, Eugene and Reifenshtein, Edward C. Jr.: The stimulating action of benzedrine sulphate; comparative study of responses of normal persons and of depressed patients. *J. A. M. A.* 108: 1770-1776, (May 22) 1937.
14. Lesses, Mark F. and Myerson, Abraham: Human autonomic pharmacology; benzedrine sulphate as an aid in the treatment of obesity. *New England J. Med.* 218: 119-124, (Jan. 20) 1938.
15. Ulrich, H., Trapp, C. E., and Vidgoff, B.: The treatment of narcolepsy with benzedrine sulphate. *Ann. Int. Med.* 39: 1212-1221, (Mar.) 1936.
16. Solomon, Philip; Mitchell, Roger S.; and Prinzmetal, Myron: The use of benzedrine sulphate in postencephalitic Parkinson's disease. *J. A. M. A.* 108: 1765-1770, (May 22) 1937.

17. Myerson, Abraham and Ritvo, Max: Benzedrine sulphate and its value in spasm of the gastro-intestinal tract. *J. A. M. A.* 107: 24-26, (July 4) 1936.
18. Myerson, A.: The effect of benzedrine sulphate on mood and fatigue in normal and neurotic persons. *Arch. Neur. and Psychiat.* 36: 816-822, (Oct.) 1936.
19. Nathanson, M. H.: The central action of Beta-aminopropylbenzene (benzedrine). *J. A. M. A.* 108: 528-531, (Feb. 13) 1937.
20. Davidoff, Eugene and Reifenstein, Edward C. Jr.: The stimulating action of benzedrine sulphate; comparative study of responses of normal persons and of depressed patients. *J. A. M. A.* 108: 1770-1776, (May 22) 1937.
21. Myerson, Abraham; Loman, Julius; and Dameshek, William: Physiologic effects of benzedrine and its relationship to other drugs affecting the autonomic nervous system. *Am. J. M. Sc.* 192: 560-574, (Oct.) 1936.
22. Robinson, Leon J.: Benzedrine sulphate in the treatment of syncope due to hyperactive carotid sinus reflex; report of 2 cases. *New England J. Med.* 217: 952-953, (Dec. 9) 1937.
23. Barger, G. and Dale, H. H.: Chemical structure and sympathomimetic action of amines. *J. Physiol. Lond.* 41: 19-59, 1910-11.
24. Council of Pharmacy and Chemistry: Present Status of Benzedrine Sulphate. *J. A. M. A.* 109: 2064-2069, (Dec. 18) 1937.

DISCUSSION

DR. LEON J. ROBINSON (*Monson State Hospital*): Dr. Cohen's paper was most stimulating and instructive. It was of particular interest to me, as both Dr. Osgood and I have been carrying out a similar study with our epileptic patients at Monson.

As Dr. Cohen has pointed out, a certain number of patients receiving phenobarbital develop drowsiness and ataxia, there being no constant correlation between the phenobarbital dosage and the incidence of toxicity.

We, also, used benzedrine sulphate in an attempt to offset the marked drowsiness and the ataxia.

With the larger doses of phenobarbital many of our patients exhibited ataxia, marked somnolence and apathy, slouching for hours in one position, a sleepy expression on their face and responding with slow labored speech. When benzedrine was given to such a patient the apathy was ameliorated and the patient became brighter.

We gave essentially the same amounts of benzedrine as Dr. Cohen used, that is, 5 to 20 mg. However, instead of giving the benzedrine over a long period of time, we continued it only as long as the patient's somnolence was evident. This meant giving the benzedrine for several days to about two weeks.

Both Dr. Osgood and I noted that the toxic effects of phenobarbital disappeared in the same length of time even if no benzedrine were given. We believe that the patient acquires a tolerance to the larger doses of phenobarbital and that, as a result, both drowsiness and ataxia disappear, but that benzedrine helps offset the somnolence while tolerance to the phenobarbital is developed.

From my own observations on the patients Dr. Osgood and I are studying, I am not yet certain that benzedrine noticeably offsets the ataxia, *per se*, produced by large doses of phenobarbital. The ataxia, like the somnolence, disappears as tolerance to the phenobarbital is established.

I agree with Dr. Cohen's statement that for the most part benzedrine has no appreciable effect on seizure incidence. The one exceptional case he reports in which additional benzedrine did decrease seizures is most striking, and indicates the rewards which may result from individualization of therapy.

In regard to the patient who died as a result of thrombosis of the internal carotid artery, I agree with Dr. Cohen's opinion that the thrombosis was not related to the benzedrine therapy.

The reduction in weight which Dr. Cohen and Dr. Myerson noted to follow the use of benzedrine is most interesting.

DR. SOLOMON: This is a most healthy difference of opinion, and I wonder if there are any other witnesses who wish to testify. Has anybody else had an experience which they wish to discuss relative to the use of benzedrine with phenobarbital?

DR. WILLIAM L. HOLT (*Worcester State Hospital*): Following the announcement of this program, I have tried this on our chronic service, on those who were having fits most frequently. I did increase the dose of phenobarbital (the majority of the cases were getting about 3 grains t. i. d.) up to $4\frac{1}{2}$ grains t. i. d. which produced ataxia and drowsiness within three days. I gave benzedrine in 10 mgm. doses morning and noon, beginning at the time phenobarbital was increased. Ataxia developed just the same at the end of the three days, and doubling the benzedrine had no effect on the ataxia that I could see. In half the cases I had to resort to cutting down the Luminol practically to the same dosage used before because of alarming ataxia. It is true that somnolence was relieved in most cases by benzedrine, and in several cases the patient is now seizure-free on a larger dose of luminol than could formerly be given. I think the regime has its usefulness and also limitations.

DR. SOLOMON: Dr. Benjamin Cohen, do you wish to say anything in rebuttal?

DR. BENJAMIN COHEN (*Grafton State Hospital*): I wish to say that our use of benzedrine sulphate in epilepsy was a secondary development. Our main and initial purpose was to adjust phenobarbital medication in a large group of epileptics to tolerance in an attempt to secure the fullest therapeutic advantage. Seizure totals for each patient and the hours of seizure incidence were reviewed weekly and at such times dosage per patient was seldom increased more than one-half grain per day for the succeeding week. Such conservatism may have prevented the development of extreme toxicity.

Drowsiness, mental dullness, and unsteadiness of gait, findings plainly attributable to phenobarbital, appeared in certain patients treated.

The first few patients treated with benzedrine sulphate for the relief of these toxic signs showed satisfactory results and were able to resume going to dining rooms far removed from their wards. Thereafter we prescribed supplementary benzedrine routinely where indicated. Reduction of phenobarbital dosage was not necessary and in combination with benzedrine we continued to employ the amounts of phenobarbital in use at the time of the development of untoward features. This was done over an average period of about four months without the recurrence of toxic findings.

I regret the necessity of disagreement but can only affirm the benefits I observed following the administration of benzedrine sulphate.

INTRAVENOUS PARALDEHYDE NARCOSIS
FOR PNEUMOENCEPHALOGRAPHY*

By LEON J. ROBINSON, M. D.
Monson State Hospital

*We wish to acknowledge the kind permission of the Editors of the New England Journal of Medicine to re-publish this paper, which appeared in that journal July 28, 1938.

Pneumoencephalography (the replacement of cerebrospinal fluid by air and subsequent roentgenography of the cranium) is often an important diagnostic aid in neurology. The procedure is distressing to the patient and often calls for deep narcosis to allay discomfort and minimize reactions. Without anesthesia, the patient experiences severe headache by the time 30 to 40 cc. of air is injected, and this becomes excruciating as more air is added. The pulse decreases to 60, 50, or even less and becomes weaker. With this there often occurs profuse perspiration, projectile vomiting, and drop in blood pressure even to shock levels, and at times collapse supervenes. As the amount of air necessary for adequate results varies from 50 to 200 cc., the air injection requires fifteen to forty-five minutes.

The pain during this long period is not only distressing to the patient but enhances the possibility of collapse and interferes with even injection of air. Threatened or actual collapse also prevents the completion of the procedure. While ether supplies satisfactory anesthesia, it produces an undesirable marked rise in intracranial pressure, which contraindicates its use in patients with pathologically elevated intracranial pressure (1).

Furthermore the rise in intracranial pressure which ether causes may prevent the filling of the ventricles with air (2). Nitrous oxide also is unsatisfactory, because, as pointed out by Waggoner and Himler (3), it increases tremendously the blood pressure and spinal fluid pressure.

In order to obviate the disadvantage of volatile anesthetics, Solomon and Epstein in 1932 (1) introduced the use of sodium pentobarbital (nembutal). This they administered intravenously (0.3 to 0.5 Gm. in 10-15 cc. of distilled water) producing anesthesia in 10-20 minutes. They also used amylal or avertin with satisfactory results. Davidoff and Dyke (2) produce analgesia by giving 3 grains of amylal orally and $\frac{1}{6}$ - $\frac{1}{4}$ grain of morphine hypodermically. In their extensive series of 4,000 consecutive encephalograms, whatever symptoms have developed have been successfully combatted by inhalations of aromatic spirits of ammonia or caffeine sodium benzoate intramuscularly. The former is used for a feeling of faintness, and the latter in case of a sharp decrease in blood pressure with slowing of the pulse.

Von Storch (4) recommended morphine grains $\frac{1}{8}$ - $\frac{1}{6}$ followed by from 0.3 to 0.5 Gm. of sodium pentobarbital intravenously. Many other barbiturates have been successfully used. However, von Storch (4) calls attention to the important fact that patients habitually using these or related compounds will be refractory to the narcotic effect of avertin, amylal, nembutal, and similar barbiturates. Thus, epileptic patients who have received regular barbiturate therapy cannot be satisfactorily narcotized with these drugs. For this group of patients, von Storch (4) administers $\frac{1}{120}$ grain of scopolamine hydrobromide subcutaneously two hours previous to pneumoencephalography, followed by $\frac{1}{8}$ to $\frac{1}{6}$ grain of morphine sulfate intramuscularly 20-30 minutes before the air injection.

The problem of a suitable narcotic, other than a barbiturate, had presented itself to the author in performing pneumoencephalography upon patients with epilepsy who receive habitual phenobarbital therapy. The disadvantages of ether and nitrous oxide were presented above. Furthermore administration of nitrous oxide often induces seizures in epileptics because of the accompanying anoxemia. While morphine and scopolamine are suitable, scopolamine occasionally causes delirium instead of sedation. The author therefore has utilized paraldehyde narcosis for pneumoencephalography in patients habituated to the barbiturates. The results were so encouraging that it has been used even in patients not so habituated. Although paraldehyde has been used previously for its anesthetic properties, we are not aware of any previous reports of its use for encephalography.

Paraldehyde ($C_6H_{12}O_6$) is a polymer of acetaldehyde. It is colorless, soluble in water, and miscible in many oils. It is quite volatile, has a characteristic pungent taste and odor, and resembles alcohol in its effect although it is a much more potent narcotic and rarely induces any symptoms of excitement. Paraldehyde is excreted mainly by the lungs and also by the kidneys. It does not depress the heart or respiration in therapeutic amounts. It has a large margin of safety. On the basis of animal experimentation Beauchemin and his colleagues (5) calculated the lethal dose for a 150-pound man to be 120 cc. of paraldehyde if given orally, or 40-60 cc. if given intravenously. Bastedo (6) states that recovery has occurred from 100 cc.

given in divided doses to an alcoholic. In an article entitled "Paraldehyde Idiosyncrasy" Brown (7) attributed a 24-hour period of unconsciousness to four drachms of paraldehyde given rectally, although it is to be noted that the patient had also received ethyl chloride and ether anesthesia.

In 1932 Rosenfield and Davidoff (8) first used paraldehyde rectally (4 to 6 drachms) to produce obstetrical analgesia. Complete amnesia for the period of labor was obtained in all but three of their patients, the latter having had partial amnesia. Less gas-oxygen was required when the head was on the perineum. The babies' breath smelled of paraldehyde for 24 to 48 hours after delivery.

Since this report there have been several reports on the use of paraldehyde in the production of satisfactory obstetrical analgesia.

Paraldehyde has also been used parenterally to produce hypnosis or anesthesia. Noel and Souttar (9) in 1912 first used paraldehyde intravenously (15 cc. of paraldehyde and 15 cc. of ether in 1 per cent cold saline). Atkey (10) in 1913 utilized Noel and Souttar's method daily for one week in a patient with tetanus. A few seconds after the medication there occurred anesthesia, followed by hypnosis and muscular relaxation. The latter persisted throughout the day, making possible the ingestion of fluids. The patient recovered from tetanus.

Since that time there have appeared additional reports on the use of paraldehyde by either the intravenous or intramuscular route. To cite but a few such reports we merely mention the papers of Johnson (11), Theodorescu and Timus (12), Nitzescu and Timus (13), Nitzescu and Iacobovici (14), and Beauchemin, Springer and Elliott (5). The latter recommend 1 cc. of paraldehyde for every 5 kg. of body weight, and have given from 5 to 19 cc. intravenously. Following the injection, anesthesia has been reported to set in within 40 seconds (9) to 90 seconds (15). The duration of anesthesia may vary from $1\frac{1}{2}$ to 21 minutes (5).

Beauchemin and his colleagues (5) believe there are few conditions which would contraindicate the use of paraldehyde, and have even used it for patients with pulmonary tuberculosis, colds, cardio-renal disease, arteriosclerosis, hypertension, diabetes, obesity, senility, and debility.

Because paraldehyde is sterile it can be injected without previous preparation and is undiluted for intramuscular use. When used intravenously it may be undiluted, in which case it should be injected rapidly (2.0 cc. per second) to prevent excitement and coughing (5), or it may be previously diluted in glucose (14), or in 1% cold saline (9).

From 1922 to 1926 Caldwell (15) had used paraldehyde intravenously to produce narcosis in 47 patients with eclampsia. He gave 1-3 cc. of paraldehyde, causing immediate relaxation and a short sleep of one to one and a half hours.

In our use of paraldehyde hypnosis for pneumoencephalography the following procedure has been adopted. Breakfast was withheld the morning of the pneumoencephalography. Sufficient paraldehyde was injected intravenously to produce deep narcosis. One-tenth of a cubic centimeter of paraldehyde was given intravenously for each pound of body weight, so that a 100-pound individual received 10 cc. of paraldehyde. However, patients weighing more than 100 pounds were not given more than 10 cc., unless this amount failed to produce the desired hypnosis. To date we have not had occasion to use more than 14 cc. of paraldehyde intravenously. Children received proportional amounts. In some instances the proportion used was two-tenths of a cubic centimeter per pound of body weight. Apprehensive or resistive patients are apt to require dosages in excess of the calculated amount. This also may hold true for chronic alcoholics.

The ante-cubital vein was used when possible. In infants, the paraldehyde was injected into the external jugular vein. Immediately after the injection was begun, the paraldehyde was excreted through the respiratory system and caused pharyngeal irritation and coughing. The patient could smell and taste the drug and the observer could recognize its odor on the patient's breath. As a rule, the patient was mildly and momentarily excited because of the sensation of "choking" due to the rapid high concentration of paraldehyde in the expired air. In two to five seconds the patient drowsed, only to be momentarily aroused by pharyngeal irritation as additional paraldehyde was injected. In the course of thirty seconds, marked somnolence developed and in 40 to 100 seconds there occurred a short period of anesthesia lasting one to five minutes. We found the anesthesia quite

brief but the deep narcosis which succeeds it is satisfactory for pneumoencephalography.

During the procedure of air injection into the subarachnoid space the patients were free of the extreme pain which the introduction of air causes. A few were totally unaware of the performance of the entire operation. The majority experienced some degree of headache but this was not marked and was well tolerated. Rarely there has been present some nausea, but there have not occurred, to date, any of the vomiting, excessive perspiration, or near collapse, such as at times may accompany pneumoencephalography. If analgesia was insufficient, morphine sulfate grains $\frac{1}{8}$ subcutaneously was given in addition to the paraldehyde. During paraldehyde hypnosis the patient retained a remarkable degree of muscle tone so that there was no sagging of the body, and the patient was easily supported in the sitting position by one assistant.

Following the injection of air, roentgenograms of the head were made, with the patient first in the vertical and then in the horizontal position. When the last plate was made the patient was placed in bed and remained in a deep sleep of 2-8 hours. On awaking he recalled nothing of the pneumoencephalography experience.

The patient did not perceive the odor of paraldehyde which persisted on his breath for as long as 24 hours. In every case recovery from the pneumoencephalography procedure was uneventful.

Beauchemin and his colleagues (5) observed that anesthesia produced by intravenous paraldehyde lowered spinal fluid pressure. This seemed to be borne out in our series of cases, the spinal fluid pressure varying between 40 and 100 mm. of water, with the patient in the horizontal position.

We noted the presence of paraldehyde in the spinal fluid following its administration, regardless of whether the route used was intravenous, intramuscular, rectal, or oral. It was identified both by its odor and by the qualitative test for its detection described in the U.S.P. XI. This consisted in heating a small amount of spinal fluid to which a little dilute sulfuric acid had been added. The latter converted paraldehyde into acetaldehyde which was recognizable by its odor.

In view of the rise in blood sugar which has been observed to follow either intravenous paraldehyde anesthesia (5) or pneumoencephalography (16), it is well to determine whether severe diabetes mellitus is present prior to pneumoencephalography under intravenous paraldehyde.

SUMMARY

The intravenous administration of paraldehyde to produce narcosis for pneumoencephalography is described.

Paraldehyde narcosis is recommended to minimize the discomfort of pneumoencephalography in patients, such as those with epilepsy, whose habitual use of the barbiturates renders them refractory to barbituric acid anesthetics.

BIBLIOGRAPHY

1. Solomon, H. C. and Epstein, S. H.: Encephalography under narcosis produced by nonvolatile anesthetics; note on technic. *J. A. M.* 98: 1794-1796, (May 21) 1932. Correction 98: 2148, (June 11) 1932.
2. Davidoff, Leo M. and Dyke, Cornelius G.: *The Normal Encephalogram*. Lea and Febiger, Philadelphia, 1937.
3. Waggoner, R. W. and Himler, L. E.: Encephalography under nitrous oxide anesthesia. *Am. J. Roentgenol.* 31: 784-786, (June) 1934.
4. Von Storch, T. J. C.: On the technique of encephalography, with special reference to use of apparatus. *Am. J. Roentgenol.* 35: 78-92, (Jan.) 1936.
5. Beauchemin, J. A., Springer, R. G., and Elliott, G. A.: Intravenous anesthesia with paraldehyde. *M. Times and Long Island M. J.* 63: 179-184, (June) 1935.
6. Bastedo, Walter A.: *Materia Medica, Pharmacology, Therapeutics, and Prescription Writing for Students and Practitioners*. 4th Ed. W. B. Saunders, 1937.
7. Brown, Gilbert: Paraldehyde idiosyncrasy; report of case. *Brit. J. Anesth.* 13: 25-27, (Oct.) 1935.
8. Rosenfield, H. H. and Davidoff, R. B.: New procedure for obstetrical analgesia. *New England J. Med.* 207: 366-368, (Aug. 25) 1932.

9. Noel, H. L. C. and Souttar, H. S.: The intravenous injection of paraldehyde. *Lancet* 2: 818-819, 1912.
10. Atkey, Oliver: A case of tetanus treated by intravenous injections of paraldehyde and copious injections of normal saline resulting in cure. *Lancet* 1: 168-169, 1913.
11. Johnson, A. S.: Parenteral administration of paraldehyde for control of pain and convulsive states. *New England J. Med.* 210: 1065-1067, (May 17) 1934.
12. Théodorescu, D. and Timus, D.: Basal anesthesia with intravenously injected paraldehyde. *Rev. de chir., Bucuresti* 38: 9-18 (July-August) 1935.
13. Nitzescu, I. I. and Timus, D.: Therapy of tetanus with paraldehyde injection. *România méd.* 13: 213-214, (Sept. 1) 1935.
14. Nitzescu, I. I. and Iacobovici, J.: Nouveau procédé d'anesthésie généralé; anesthésie de base par injection intraveineuse de paraldehyde glucosée. *Presse méd.* 42: 331-333, (Feb. 28) 1934.
15. Caldwell, W. E.: The intravenous use of paraldehyde in eclampsia. *New York State J. Med.* 26: 57-58, (Jan. 15) 1926. Report of a fatal case of epilepsy and two cases of chorea in pregnancy. *Am. J. Obst. and Gynec.* 2: 555-558, (Sept.) 1921-22.
16. Scott, Michael: Cure for sugar content of blood following encephalography: comparison with usual curve for dextrose tolerance. *Arch. Neurol. and Psychiat.* 38: 985-991, (Nov.) 1937.

DISCUSSION

DR. ROGER G. OSTERHELD (*Taunton State Hospital*): The paper which we have just heard is an original work as far as I can find from a survey of the medical index. During the last ten years very little work has been done in intravenous paraldehyde, and none has been reported showing the use of paraldehyde in pneumo-encephalography. I think we owe Doctor Robinson a vote of thanks for the pioneer work which he is going.

In a hospital for epileptics we run into a different problem than we find in other state hospitals. The use of phenobarbital is not as common, and it does not have to be taken into consideration as often as in an epileptic hospital.

During the last ten years there has been only one case reported showing idiosyncrasy to paraldehyde. This was a case in Australia, and was described in the *British Journal of Anesthesia*. The patient was critically ill for twenty-four hours with markedly increased temperature, congestion of the lungs, and loss of all reflexes, but recovered without after effects. Because of the apparent freedom from toxic effects, and the few cases of idiosyncrasy, paraldehyde, with its wide margin of safety, is a safe drug to use. The intravenous and parenteral injections should be used entirely in the hands of physicians; as it is such a safe drug to use, there may be some lessening in the precautions which are necessary.

Paraldehyde was introduced by Cervello in 1882. Since that time there have been periods when it was widely used, and other periods when it was in disfavor. The reason for this is not because of the action of the drug on a patient, but because of its effect on the other patients on the ward where it was used. There are a few counter indications for paraldehyde. These have been mentioned by Doctor Robinson. There is one addition which should be made to these counter indications, however, and that is in the case of the patient receiving iodides, paraldehyde should not be given.

The tolerance to paraldehyde varies with the different individuals. The dose has to be increased as time goes on. In about two per cent of the patients there is a short period of violence or disturbance, but the time is so short, being only about half a minute, that this can easily be controlled.

Doctor Robinson spoke about some of the after effects due to paraldehyde. To this should be added the possibility of a rash, which may be severe in some patients. At times there is ulceration of the mucous membranes, especially of the nose, and occasionally patients have epileptoid convulsions. These have not proven fatal in any case, and would not be severe enough to stop the use of paraldehyde.

At the February meeting of the Boston Society of Psychiatry and Neurology a paper was read concerning the use of barbiturates and paraldehyde. It is claimed that the barbitol group cause symptoms similar to those seen in multiple sclerosis,

i.e.: nystagmus, absence of abdominal reflexes, ataxia, and slurring speech. It is also claimed that there is a strong linking of the barbitol group to the nerve cells. On the other hand paraldehyde did not show neurological symptoms because of loose linking with the nerve cells. The complete amnesia following the use of paraldehyde allows procedures to be completed without the knowledge of the patient. The lack of relaxation of the muscles is very much of an aid in pneumoencephalography, and also in many other surgical procedures.

The big drawback in the use of paraldehyde is its odor. This is disagreeable in nature, fusel oil odor in character, and it permeates throughout the ward, and even throughout the whole building. If there was some manner in which the odor could be eliminated or covered, the use of paraldehyde would probably be much more common than it is at the present time.

DR. BENJAMIN COHEN (*Grafton State Hospital*): For several years we have been using paraldehyde by intramuscular injection with great satisfaction. There were several features relative to intravenous administration of the drug which appealed to us, but we felt a natural reluctance to use the drug in this fashion since we realized that we were dealing with a stock preparation not specially designed for parenteral use.

We contacted one of the manufacturers of paraldehyde in regard to the matter and were informed that it was their belief that the drug was sterile in itself. Since the answer seemed a bit vague we decided to check upon the matter ourselves. We added 15 cc. of stock paraldehyde to 75 cc. of sterile hormone broth and incubated the mixture forty-eight hours. Gram-stained smear from this culture revealed no organisms. Blood plate was then inoculated from culture and incubated twenty-four hours. No growth appeared. After fifty-two hours sterile culture was again examined and Gram-stained smear revealed as before absence of organism. A blood plate was again inoculated from culture and no growth was obtained. We concluded that this preparation of stock paraldehyde was sterile.

Then we studied the effect of stock paraldehyde upon a streptococcus blood culture. Ten cc. of blood obtained from a patient with streptococcus septicemia was added to 75 cc. of sterile hormone broth and to this was added 15 cc. of paraldehyde. After forty-eight hours of incubation Gram-stained smear from culture revealed absence of organism. Blood plate inoculated from blood culture showed no growth after twenty-four hours of incubation. Blood culture was examined fifty-two hours later. Stain of smear obtained from culture was negative for organism and blood plate inoculated from culture and incubated twenty-four hours showed no growth.

Control blood culture (containing no paraldehyde) revealed these findings: Gram stain of smear from culture showed many Gram positive cocci in short chains. A blood plate was inoculated from culture and in twenty-four hours there were many small grayish-white colonies surrounded by zones of hemolysis. Gram-stained smear from blood plate demonstrated the presence of many Gram-positive cocci in short chains.

We concluded that stock paraldehyde in the dilution mentioned had a sterilizing effect upon streptococcus hemolyticus.

DR. LEON J. ROBINSON: The intravenous use is necessary if you are to get the immediate effect at the time you are about to use pneumoencephalography, just as in giving nembutal intravenously. Paraldehyde can be given intramuscularly, but if the patients have not had previous sedation, it is painful. It is more convenient for the patient to have it intravenously.

DR. SOLOMON: Some ten years ago or more Dr. C. Macfie Campbell read about the use of intravenous paraldehyde as an hypnotic. I don't know whether he remembers the occasion, at the American Medical Association, in relation to treatment of mental disease. It was his suggestion that we try intravenous paraldehyde in handling acute maniacal states, and, as Doctor Robinson points out, the effect is almost immediate. It is a matter of a second. It is followed by choking, coughing, and then very suddenly a very nice quiet sleep.

DR. C. MACFIE CAMPBELL: We used it for a certain period at Boston Psychopathic Hospital for acute excitement.

THE ATTENTION DEFECT IN SCHIZOPHRENIA,
ITS GRADATIONS AND THERAPEUTIC IMPLICATIONS

By B. H. FLOWER, M.D. and BENJAMIN COHEN, M.D.

Grafton State Hospital

Probably at no time in the history of psychiatry has there been such widespread genuine interest in the problem of schizophrenia as has been evidenced during the past year. This interest has of course been stimulated by the reports of successful therapeutics from a large number of workers, abroad and in this country. Yet there is no unanimity as to criteria for the diagnosis of the condition, with the result that the term is often applied with scant evidence in support, applied in intuitive rather than in reasoning fashion. In part this has been due to obscure etiology and somatic pathology; in part due to lengthy and indefinite delineation; in part due to a feeling that the syndrome brought together a strange set of bed fellows only distantly related to one another if at all. Rosanoff has reflected this chaotic situation in the 1938 edition of his text where he states that he has been "compelled by the nature of things" to omit schizophrenia as an entity.

Certainly, if we are to accept schizophrenia as a working hypothesis until newer knowledge shall further clarify the situation, there must be reasonably clear-cut criteria for the awarding of the diagnosis. Otherwise the label conveys little definite meaning, our statistics are grossly inaccurate, and reports of particular findings within the group mean little or nothing.

For several years at Grafton we have been endeavoring to outline a delineation of the syndrome for our own use, to the end that the diagnosis might be consistently arrived at and consistently defended among ourselves. It has seemed to us that there were certain features common to all schizophrenics and that logically one should first identify the patient as schizophrenic before considering a diagnosis of paranoid schizophrenia or any other sub-group. These basic features are considered to be (1) a predominance of imaginative thinking which results in (2) impairment of attention and (3) disturbance of affect as accorded reality. The term "imaginative thinking" is used to refer to phantasy, imaginative believing (delusions), and imaginative perception (hallucination). The attention of the patient tends to be fixed to the imaginative thought content in such a way that spontaneous shift to reality is handicapped. Furthermore, the attention focus strongly conditions the affective display.

In dealing with schizophrenics by the usual methods of approach and therapeutics in the hospital, this inattention to reality is a major barrier. For the purposes of studying inattention, the chronic population of a mental hospital offers excellent material. Features recognized in marked degree in them may be detected in early, rudimentary form in the cases of recent onset.

Now, what are the forms of inattention displayed by the schizophrenic? First, regarding stimuli received by the special senses: He averts his eyes from the examiner, he closes his eyes, he seeks an environment best suited to exclude such stimuli (remote, dark corners of the ward, envelopment of the head in blankets, etc.). Ears may be blocked to exclude environmental sounds. (Said one of our patients, "I get my messages best that way.") There may be disinterest in conversation and radio programs or seclusive retreat to spots suitable for preoccupation. To the quality, seasoning, and taste of food there is relative indifference. Odors evoke slight response, floral pieces no appreciation, feces no protest. Tactile sensations appear diminished. There is increased tolerance to pain and physical discomfort, unconcern for factors normally contributing to bodily ease.

Secondly, relative to the organic sensations, visceral and kinesthetic: Stimuli arising from the gastrointestinal, cardio-respiratory, and genitourinary systems are often accorded relative disregard. The appetite may be impaired; intestinal colic, constipation, diarrhea, and hemorrhoids are frequently unheeded; chest pain, cough, palpitation, dyspnea, and allied symptoms evoke unconcern. Likewise, dysuria, retention, frequency, leukorrhea, and menstrual disorders seem unheeded. These patients are sometimes seen in uncomfortable maintained postures or repeating meaningless gestures over and over again without evidence of fatigue.

Thirdly, relative to the conventional patterns of thinking of the time: Unless these phases represent a part of the imaginative scheme, patients are prone to give scant attention to ethical, moral, and religious codes. Devotion to parent, to offspring, or to marital partner is often scant. Education, current events, politics, employment, ambitions are relegated to the background.

Fourthly, relative to customary patterns of behavior: Social, self-preservative, and sexual interests are definitely impaired. The habit of seclusiveness facilitates

the patient's exclusion from society; he has no desire to participate in group activities. The etiquette of eating may be disregarded. Fingers replace utensils; food is bolted, stolen from nearby fellows, smeared over the face and clothing. Urinary and fecal untidiness, carelessness of dress, and unconcern in the presence of danger are often seen. Inability to engage in occupation, unconcern for the requirements of life (shelter, clothing, food, warmth, etc.), neglect of dependents, assaults upon others, and lack of constructive attitude necessitate supervision and protection. It is generally observed that reproductive tendencies are lost or greatly diminished. Sexual behavior becomes chiefly confined to autoeroticism or passive homosexuality.

Fifthly, relative to the requirements for normal thought expression: The schizophrenic's paragraph and sentence construction commonly lacks unity, coherence, and proper organization. This, coupled with vague word selection and neologistic trends, results in disjointed sentences and scrambled paragraphs. These tendencies are particularly evident in spontaneous speech and in unguided writing.

These maladaptations to reality and many more are to be found in a chronic schizophrenic population. It seems to us that preoccupation with imaginative thinking, causing impaired attention to reality in its various phases, is a basic fault in this syndrome.

The gradations of attention defect and therapeutic implications hinge upon the fact that attention is not completely or continuously bound to imaginative thinking. The profoundly deteriorated patient shows inattention to reality in its most complete form. One sees in each patient a constant bidding of reality against imaginative content for attention. Since attention tends to be fixed to imaginative thinking in such a way that spontaneous shift to reality is handicapped, it follows that anything which forces reality upon the patient should be of therapeutic benefit.

Some patients are aware of this conflict of bidding. Said one man (R. R.) "Doctor, while you're talking with me I don't hear those voices," (homosexual accusations). Other factors favoring temporary displacement of imaginative thinking are many. During the process of questioning, strength, selection, and repetition of stimulus are used to gain attention. One patient (A. P.) when asked the name of the place, replied, "Formosa Tea House." But finally after much repetition and tapping on the shoulder, he coyly responded "Grafton State Hospital." One of the authors (B. C.) used as his initial bid for attention an appealing stimulus, the proffering of candy to catatonics at each ward round. This gradually led to the drinking of milk, the resumption of eating, and other activities. Another adaptation of this type of stimulus is the use of music, movies, entertainments. In our class for deteriorated patients at the Grafton State Hospital, piano and a few large rubber balls evoked surprisingly appropriate responses.

Conditions favoring displacement of reality tend to produce a situation reverse to that just mentioned. In questioning, a provocative test is sometimes employed. The patient may be directed to listen carefully while the examiner remains silent in order that displaced abnormal mental content may again assert itself. After a time he may announce that he hears the accusing voices anew. One frequently asks the patient if he hears voices at night. This is tacit admission of the fact that with environmental stimuli at a minimum, reception of stimuli of imaginative origin is facilitated. In day-time activities one may detect ample evidence of schizophrenic's attempt to exclude reality in favor of psychotic content. This tendency is shown by the covering of the head with blankets, the seeking of remote spots, the obstruction of ear canals by various means, etc.

Keeping in mind this bidding of reality against psychotic content for attention, let us recall that rather large, unprepossessing group of patients present in every mental hospital. Their spontaneous speech and writing show definite attention defects; they are completely satisfied with indolence. Certain of them are capable of useful employment under direction. In an attempt to statistically estimate the facility of attention shift in such patients an adaptation of the Jung Word Association Test has been employed. The routine list of 100 non-specific words was used. Replies to the stimulus words were grouped as indicating attention or inattention. Any logical association, spelling of the word, or a definition thereof were accepted as evidence of attention. Those responding with a high degree of relevant replies were found capable of worthwhile directed work.

An example is J. C. No. 6785 (Schizophrenia, Paranoid Type, age 49, hospitalized 14 years). This patient is reasonably neat, generally coöperative, has auditory hallucinations, grandiose and persecutory beliefs. He is well oriented; I. Q. 99. Staff Meeting notes state: "So long as the topics were kept on every-day matters he gave relevant, pertinent, correct answers. . . . He showed excellent orientation and memory with a surprising retention of school and general knowledge. . . . When asked why he had been hospitalized—he lapsed into an involved, incoherent, irrelevant speech." A sample of his spontaneous speech is as follows: "I hear paranoid voices de the instruments radio—I hear paranoic talk from radialis naturalism de premeditation than de nom sperio de Cummings de Fall River who through framery it lie as name is physician. . . . in mentis de mind de naturalism de alienism has caused me to be put in hospital." This patient's responses to the word association test were as follows: 60 acceptable English words; 15 correct Latin expressions (brother—frater, head—caput, water—aqua, stem—stamen, etc.). 25 relevant neologisms (to sleep—somniize, to swim—aquaate, dead—mortuize, etc.). All these replies were interpreted as indicative of attention. He has parole, has been found to be a good bed maker and dining room worker. Left to his own devices he would spend his entire time translating magazines into what he calls Roman Latin.

Another example: A. S. No. 6819 (Schizophrenia, other types, age 60, hospitalized 20 years). A sample of spontaneity is "Dead spirit listing on head for thoughts to express to party around as an inven of a mental screatet nedds of a." He experiences auditory hallucinations; a spirit comments on his thoughts, which are repeated by radio. Promiseous women call to him, keep him in temptation, and assist dead spirits in prolonging his condition. Test as applied to him revealed 96 per cent relevance and 4 per cent irrelevance. He has proven to be a good dining room worker.

J. M. No. 3418 (Schizophrenia, Catatonic, age 58, continuously hospitalized since 1906.) He is untidy in appearance, noisy and destructive at times. He admits auditory hallucinations and delusions of wealth, gives his age as 17. His spontaneous speech is irrelevant and incoherent. His test results by word association show 41 per cent relevance and 59 per cent irrelevance. Examples of his irrelevance are lead pencil—he knows he was born here; new—at home; to prick—long street; frog—Dave told you, etc. At times he would simply grunt or nod instead of offering an association. This patient is limited to floor swabbing under close supervision.

A. P. No. 2605 (Schizophrenic Catatonic, aged 54, hospitalized 30 years). He is uncoöperative, inattentive, careless in appearance, experiences auditory hallucinations. Cannot give his age or the season, but does correctly identify the ward upon which he resides. Attempts to apply word association were unsuccessful. To all stimuli the patient responded with a stereotyped "Yes" or nodded his head while staring into distance. All efforts to interest him in any type of occupation have failed.

These four examples represent gradations in schizophrenia as demonstrated by an adaptation of the Jung Word Association Test. Our experience with the test over a period of years confirms our initial impression that it is useful as a means of statistically indicating the degree of impairment of attention to reality, and of selecting patients suitable for employment under direction. It is not unreasonable to suppose that this test may be satisfactorily employed to indicate the degree of progress shown by patients receiving special therapy of any type.

SUMMARY

1. A practical delineation of the fundamental features of schizophrenia is presented.
2. Emphasis is laid upon the schizophrenic's defect attention to reality. This defect is seen in relation to (a) special sensory stimuli; (b) organic, visceral and kinaesthetic sensations; (c) conventional patterns of thought; (d) customary patterns of behavior; (e) the requirements of normal thought expression.
3. Under varying circumstances the attention may be disengaged from abnormal thought content to realistic stimuli.
4. To select patients capable for work assignment, an adaptation of the Jung Word Association Test has been used. This constitutes a test situation wherein

words are employed as an example of reality and the patient's ability of relevant response is accepted as his probable competence to cope with simple objective situations.

5. Patients with high test ratings, despite appearances to contrary, are generally capable, under supervision, of handling analogous situations in nature of work.

6. The test offers a means of statistically recording the degree of the patient's defect of attention to reality and in that connection may be of value in charting progress under special therapy.

CONCLUSION

In identifying the basic schizophrenic syndrome and in choosing therapeutic approaches, fundamental features must be recognized. In this way one may avoid confusion by minutiae in diagnosis, and in therapy one may escape commitment to any single therapeutic procedure which may attract fancy at the moment. Recalling that attention defect may be expressed in a variety of ways, which have been outlined, one may plan the therapeutic approach accordingly. One may choose from many avenues of appeal: special sensory, visceral, intellectual, instinctive, and emotional. Viewed in this light, the religious activities in the hospital, the occupational therapy, music, recreational activities, industrial employment, athletics, etc., all become coördinated factors directed toward the focusing of attention upon reality at the expense of competitive imaginative thought content.

DISCUSSION

DR. WILLIAM L. HOLT (*Worcester State Hospital*): Dr. Flower has given us a well-written presentation of what he and the group at Grafton mean by schizophrenia, which they condense into the formulation that it is a splitting of attention between the reality situation and the patient's imaginative world. No doubt this is a very important and perhaps the central problem in the schizophrenic patient. I think few of us would limit our conception of schizophrenia to just this statement, however.

I can think of a group of simple schizophrenics who show refusal to work, laying down of the responsibility that they should be carrying. These patients may give highly relevant replies when given a Word Association test, and yet be utterly worthless in terms of productive work in society and also in the hospital group. There are other obvious exceptions to the direct correlation of relevantness in reply to word association tests and job success in the hospital. There is that group of paranoid schizophrenic patients who can converse very relevantly with you, but refuse to work because they own the institution, or because they have simply made up their minds that they have done their share of work, and other people are going to work for them.

I think there is no direct correlation between relevantness of reply and actual work of the patient. It is true that some patients who give no attention to the examiner, who speak about their own preoccupations when faced with a test situation, are in general worthless to the hospital in the economic sense. It is also true that other people giving relevant replies may also be worthless. Another exception is that group of patients who may be entirely mute, refuse to say anything in the test situation whatsoever, turn and walk away from the examiner, refuse to be interviewed at all, yet be very effective workers, and I can think of several who work here at Worcester State Hospital as masons building stone walls, doing fairly high class labor. These patients would be scored as nil as far as relevant replies go, yet certainly are productive and a distinct economic asset, taking the place of paid employees.

The word association test can give a numerical answer to the degree of coöperation of the patient at that particular interview. I think it gives little else when the responses are not analyzed any further except as to whether or not it is some sort of reply that may be a definition or in the opinion of the examiner is in some other way relevant. We are given no statement as to whether or not a different examiner would consider the same reply irrelevant. The psychologist has perhaps had the most experience in dealing with word association tests, and he has found it necessary as a guide to him to have a series of words which are frequently found statistically in reply to the test word among a thousand normals so that when a patient gives a word it can be said to be a common response or particularly rare or quite unique.

Furthermore, I think the author has not given us information to indicate how the test performance correlates with any particular type of job. That might be the limitation of time imposed upon any speaker, and of course, some papers are presented here in a preliminary fashion, statistical data being reserved for later publication in detail. I think there are several questions, some of which I have pointed out, that we will want to have answered. We need to know how the patient's test performance varies from day to day, or in different phases of his illness, as he gets worse, as he gets better, when he works, when he refuses to work.

I think that statistical evidence on these problems needs to be presented before we should use the word test and the gross relevance of response as a definite criterion for improvement with special therapies.

DR. LOUIS H. COHEN (*Worcester State Hospital*): I was very much interested in Dr. Flower's presentation since it has relevance to a problem in which I have long been interested and for which, from my experience, some corroborative evidence can be adduced (*J. Ment. Sci.*, Mar. 1938). He has emphasized the point of view that the excessive preoccupation of the schizophrenic with imaginative productions to the exclusion of external reality is indicated by difficulties in the attention mechanism. I agree that the attention difficulties depend upon the fundamental difficulty of creative imagination. Dr. Flower suggested that there occurs a change in the imaginative processes from those which deal with external reality to those which deal with the patient's body in terms of gastro-intestinal or gastrourinary function, for example. This offers a clue as to what may be at the basis of the change in the patient's imaginative productions. This basis appears to be the change in the patient's preponderating imagery. An individual's imagery deals with external reality (visual, auditory), or with his own body (kinesthetic, tactual-temperature, olfactory-gustatory). It has been shown in a series of twenty-one cases, with an imagery-test not unlike the Jung Association Test, that there is a definite difference in the imagery of normal and schizophrenic individuals. There is a relative loss of visual and auditory imagery in schizophrenics and a relative gain in kinesthetic and/or tactual-temperature or olfactory-gustatory. The inference is then that, under such conditions, the nature of the attention difficulty is not one of defective attention, but rather represents a change in the direction of attention. This change arises from change in the imagery of external reality to that of imagery of the body. The patient's attention is directed less upon the world and more upon himself. One sees in this formulation the evidence of what the psychoanalysts call increased narcissism.

Further proof of the significance of changes of preponderating imagery in schizophrenics is found in the nature of the specific clinical symptomatology.

Dr. Flower's use of his testing procedure for diagnostic and therapeutic purposes makes his observations not only of theoretical interest but also of considerable practical value.

DR. C. MACFIE CAMPBELL (*Boston Psychopathic Hospital*): Dr. Flower has plunged us into the field of schizophrenia and of course there is no limit to the topics one might take up. I just want to make one or two remarks. Dr. Flower has referred to attention. Attention and interest are very closely related; a special deficiency of interest is what Jung would put at the basis of schizophrenia as its most fundamental symptom, and as equivalent to interest he would use the term libido. Some patients show very little attention, they are not responsive. The activity of the individual involves spontaneity and response; the individual reaches out for stimuli in order to express itself, and the individual is responsive to stimuli coming independently from the outside world. In some of our patients we are struck primarily with the lack of spontaneity.

In Organic Brain Disease there is frequently a lack of attention. The patient shows no reaching out, no spontaneity. Some schizophrenics who have changed from alert high school students show no spontaneity and little attention to various stimuli; one wonders whether if in this group there is not some subtle organic process.

What especially strikes us in many a schizophrenic is his lack of attention to those topics which most naturally elicit our attention, topics of interest in relation to the various issues of life. It is not the lack of attention, but rather a distorted

or unusual or very individualistic and sometimes exaggerated attention. Take the Rorschach Test; the schizophrenic may pay attention to unusual details, just as with his special interests he shows a distorted attitude towards the fundamental aspects of life. Now these fundamental aspects of life are the social ones, the aspects of life which help us to fit in well with the group and with regard to which the normal endowment of the individual is utilized in a well-balanced way. In the schizophrenic it is not so much the general reduction of attention as the direction of the attention, the distorted selectivity of attention, the complex determination of the attention which is outstanding. There is frequently no significant general loss of attention or interest any more than there is a fundamental loss of affect.

Some schizophrenics show no interest in their routine environment but respond to new opportunities. I think we learn a good deal from the observation which was registered thirty years ago by a Swiss psychiatrist, that chronic patients when transferred to a new institution may show a surprising renewal of interest and general improvement. I think Dr. Flower has brought to our attention a topic of very great interest, one associated with the most fundamental problems of this whole clinical group.

DR. SOLOMON: Dr. Flower, do you wish to make any remarks?

DR. FLOWER (*Grafton State Hospital*): In formulating the concept which has been offered, attention has been defined simply as "the assumption of an attitude best suited to the reception of stimuli." The attitudes of the normal individual and the schizophrenic differ because the former spontaneously assumes a position best suited for the reception of special sensory and other realistic stimuli whereas the latter favors imaginative stimuli. The attention of schizophrenic patients tends to be fixed to their imaginative thought content, but such fixation is not constant at all times nor is it generally complete. We pointed out that there is continual competitive bidding of reality and of imaginative thinking for attention and that the shift of attention to matters realistic may be influenced, either favorably or unfavorably, by various means. The objection has been raised that this concept is not applicable to certain types of schizophrenia, notably the simple and paranoid groups. There immediately arises the question of differential diagnostic standards. Probably many cases classified as paranoid schizophrenics, for example, could not be accepted as such if the criteria which we suggest were applied. The adaptation of the Jung Word Association Test does not represent the test as it is characteristically employed. We have used it simply as a means of estimating the degree of attention accorded the stimulus words, as judged by the percentage of relevant responses given. We have used it as a means of selecting worthwhile workers from large groups of unprepossessing patients. We have found that those capable of rendering a high percentage of relevant associations have been likewise capable of focusing attention under supervision on work projects. It has occurred to us that this adapted test method might be of value in grading improvement of attention to reality in patients undergoing any of the special therapies.

DR. SOLOMON: I think the attention of the group has been extraordinary today and merely indicates the high grade of communication we have heard today, and which I think was certainly a revelation in one sense, and a great sense of satisfaction in another. I think the old statement, "Massachusetts, here she stands," is worthwhile, and I think we would like to have farewell from Dr. Bryan, who got us together.

DR. WILLIAM A. BRYAN: I have just one announcement to make before wishing you Godspeed. We hope to have a special number of the Bulletin containing the entire transactions of this meeting. I believe the readers have agreed to submit their papers to the Bulletin, and while it may not appear for a month or two, sooner or later through the coöperation of the Department we shall have the special number. There will be a sufficient number printed so that all hospitals can submit a large mailing list.

I think you will agree with me that this is an opportune time for putting out transactions of this kind. If we ever needed bolstering up, I am sure it is at the present time. I wish to thank you all for your attention and coöperation. I hope you have enjoyed the sessions. The large share of the credit for the arrangement of this meeting is due to Doctor Cameron, and I make due acknowledgment to him. I hope that we may get together frequently on a program similar to this.

